Adjustment for the measurement error in evaluating biomarker performances at baseline for future survival outcomes: Time-dependent ROC curve within a joint modelling framework

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Abstract

The performance of a biomarker is defined by how well the biomarker is capable to distinguish between healthy and diseased individuals. This assessment is usually based on the baseline value of the biomarker; the value at the earliest time point of the patient follow-up, and quantified by ROC (receiver operating characteristic) curve analysis. However, the observed baseline value is often subjected to measurement error due to imperfect laboratory conditions and limited machine precision. Failing to adjust for measurement error may underestimate the true performance of the biomarker, and in a direct comparison, useful biomarkers could be overlooked. We develop a novel approach to account for measurement error when calculating the performance of the baseline biomarker value for future survival outcomes. We adopt a joint longitudinal and survival data modelling formulation and use the available longitudinally repeated values of the biomarker to make adjustment of the measurement error in time-dependent ROC curve analysis. Our simulation study shows that the proposed measurement error-adjusted estimator is more efficient for evaluating the performance of the biomarker than estimators ignoring the measurement error. The proposed method is illustrated using Mayo Clinic primary biliary cirrhosis (PBC) study.

Keywords: time-dependent ROC curve, joint modelling, baseline biomarker, measurement error, PBC

1. Introduction

Due to current trends in medical practice towards personalised medicine, biomarkers have grown in importance in clinical studies. More and more studies are conducted to discover biomarkers that can accurately signal a clinical endpoint, e.g. measures of liver function such as prothrombin index as indicators of liver fibrosis [1], and in clinical practice, rapid tests of biomarkers hold the promise of prompt diagnosis of diseases for an improved outcome, e.g. sepsis [2]. In this article, we refer the term "biomarker" to a single biomarker such as prothrombin index or to a composite risk score. A good biomarker can help identify patients who will have an early clinical benefit from a treatment or effectively guide the choice of therapeutic decisions, improving patients survival. However, due to imperfect laboratory conditions such as operator error, contamination, variable storage conditions, and limited machine precision, biomarkers are often subjected to substantial error in studies [3]. Failing to adjust for such measurement error may hinder the explanatory power of the biomarker, and in a direct comparison, useful biomarkers could be overlooked due to measurement error [4,5].

The performance of a biomarker is based on how well the biomarker is capable of discriminating between individuals who experience the disease onset (*cases*) from individuals who do not (*controls*). It is usually quantified by receiver operating characteristics (ROC) curve analysis, a well-established methodology in medical diagnostic research [6]. The area under the ROC curve (AUC) is an effective way to summarise the discriminative capability of the biomarker. AUC takes values from 0 to 1, and a biomarker with high AUC is considered better. A single biomarker value at baseline is mainly used in this assessment. Baseline time is an important time horizon in practice, as it is considered as the earliest time point of the patient follow-up time and provides the time base to assess the disease progression. However, individuals who are free of disease at baseline may develop the disease later in the follow up, and therefore, the assumption of fixed disease status over time may not be appropriate when evaluating the biomarker performance. Hence, incorporating the time dimension in ROC curve analysis has recently been actively researched, enabling better clinical guideline in medical decision based on biomarkers. The time-dependent ROC curve is usually derived from risk regression models such as Cox proportional hazards model as they naturally account for censored failure times. This ROC curve estimates the performance of baseline biomarker at future time points. For example, in a breast cancer study, time-dependent ROC curve was used to assess whether the patients are free from subclinical disease if the clinical disease does not emerge by two years of screening [7]. It has also been used to assess the predictive ability of the gene expression signatures in detecting early tumour response among metastatic colorectal cancer patients [8]. Lu et al. [9] identified a robust prognostic biomarker for tumour recurrence among lung cancer patients using time-dependent ROC curve analysis by estimating the AUC of the 51-gene expression signature at 60 and 100 months of follow-up. Using time-dependent AUC, Chen et al [10] made direct comparison of five recently recognised serum biomarkers and identified those can be recommended for use in clinical practice to surveillance of cirrhosis for hepatocellular carcinoma patients. A comprehensive review of current time-dependent ROC curve analysis approaches is provided by Kamarudin et al. [11]. However, Faraggi [12], Reiser [13] and others concerned about ignoring the measurement error of biomarker values in ROC methodology, and showed that the effect can be substantial on the decision as to the diagnostic effectiveness of the biomarker.

As discussed by Henderson et al. [14] and many others, a framework such as joint longitudinal and failure-time outcome modelling is capable of avoiding biases not only due to informative missingness in biomarker measurement schedule, but also due to measurement error. In a joint model, both longitudinally repeated biomarker and censored failure-time processes is modelled simultaneously. This novel modelling framework has rapidly been developed in the past decade (see Gould et al. [15] and Tsiatis and Davidian [16] for comprehensive reviews of the model). Many have adopted or extended this framework to investigate the association between the biomarker and the hazard of failure (e.g. [17]), or to derive risk predictions (e.g. Proust-Lima and Taylor [18], Garre et al. [19]). However, adopting the joint models for estimation of diagnostic effectiveness of a biomarker has been limited. Kolamunnage-Dona and Williamson [20] used joint modelling framework to evaluate time-dependent discriminative capability of a biomarker within the ROC curve analysis. In other studies, ROC curve has been used to evaluate the accuracy of the predicted survival probabilities from the joint model (e.g. Rizopoulos [21]). Henderson et al. [22] has parameterised the underling association between longitudinal biomarker and failure-time processes by individual-level deviation of the longitudinal profile from the population mean, but R^2 like statistic is used to quantify the predictive accuracy of a biomarker for failure rather than the ROC curve.

According to our review [11], measurement error of the biomarker has been ignored in all current time-dependent ROC curve approaches. And, to our knowledge, joint modelling framework has not been adopted to make adjustment for measurement error when evaluating the performance of the biomarker in ROC curve analysis. As its main contribution, this article provides a new development of time-dependent ROC curve to evaluate the performance of baseline biomarker correcting for the measurement error. We propose to utilise a joint model to link the baseline biomarker and failure-time process, and use the individual-level deviation of the biomarker from the population mean to develop an estimator to evaluate the time-dependent ROC curve. In health research, often biomarkers are recorded longitudinally as patients are followed up over time, and we use available longitudinal measurements of the biomarker to make adjustment of the measurement error in our proposed approach. By incorporating the longitudinally repeated biomarker measurements, we make the most efficient use of the data available.

2. General notation

Let T_i be the true failure time (e.g. time to death or time to disease onset) for the ith individual. Let $\delta_i = I(T_i \leq C_i)$ be the indicator of the failure, taking values 1 if the failure is occurred at time T_i, and 0 if it is not occurred, so censored at time C_i. We observe the failure-time process $\{X_i, \delta_i\}$ where $X_i = \min(T_i, C_i)$ defines the observed failure-time for $i = 1, \ldots, n$ individuals in the study dataset. Let $\boldsymbol{y}_i =$

$\{y_i(t_{ij}), j = 1, ..., m_i\}$ be a set of all available biomarker measurements recorded at times $t_{ij}, j = 1, ..., m_i$ for the ith individual. y_{i0} is the biomarker measurement of the ith individual at baseline level (observed at baseline time $t_{i1} = 0$).

3. Estimation of measurement error-adjusted estimator of baseline biomarker

Firstly, we formulate the joint model. A joint model is usually consisted of two submodels; a submodel for longitudinal measurements of the biomarker $\boldsymbol{y}_i$ and a submodel for failure-time $\{X_i,\delta_i\}$. The two components are linked together through some shared parameters. Longitudinal data are typically modelled by linear mixed effect models, while the failure-times assume various choice of modelling approaches through shared latent effects [15]. In general, a Gaussian linear model is assumed for longitudinal data, and proportional hazards is assumed for failure-times. Through the joint model, we can link the true (without measurement error) biomarker trajectory and the hazard of the failure for each individual. We follow joint modelling approach proposed by Henderson et al. [14], but as we only consider that the baseline value of the biomarker is predictive of the failure, we formulate the joint model by

$$\begin{aligned} y_{ij} &= \beta_0 + \beta_1 t_{ij} + U_{0i} + U_{1i}t + \varepsilon_{ij} \\ \lambda_i(t) &= \lambda_{0i}(t)\exp(\gamma U_{0i}) \end{aligned} \tag{1}$$

where U_{0i} and U_{1i} are individual-level random intercept and random slope respectively, and they reflect the true difference between longitudinal profile of each individual from the population mean. In particular, U_{0i} reflect the true deviation of the biomarker value from the population at baseline time. Therefore, through U_{0i}, the proposed submodel for failure-time links the risk of failure directly on the *true* scale of the biomarker at baseline for each individual. We assume (U_{0i}, U_{1i}) follows a bivariate normal distribution with mean 0 and variance $\Sigma_u = \begin{pmatrix} \sigma_{u_0}^2 & \sigma_{u_0,u_1} \\ \sigma_{u_0,u_1} & \sigma_{u_1}^2 \end{pmatrix}$. In the joint model, the measurement error process is accounted for by ε_{ij} in longitudinal data submodel. The measurement error process is non-differential and can be defined by a classical additive measurement error model $y_{ij} = y_{ij}^* + \varepsilon_{ij}$ where y_{ij} is the error-prone measure of y_{ij}^*. We assume ε_{ij} follows a Gaussian distribution with mean zero and variance σ_ε^2. The above longitudinal data submodel assumes that in the absence of measurement error, the biomarker follows a perfectly linear trajectory. In failure-time submodel, $\lambda_{0i}(t)$ is an unspecified baseline hazard, and γ estimates the level of association between baseline biomarker and hazard for the failure.

We can estimate the model by maximising the joint likelihood of the observed data via the Expectation-Maximization (EM) algorithm [5, 11]. The EM algorithm involves taking expectations with respect to the unobserved random effects U_{1i} and U_{0i}, and it iterates between two steps (E and M) until convergence is achieved. For the proposed joint model, E-step determines expected values $E[U_{0i}]$ conditional on observed joint outcome $\{\boldsymbol{y_i}, X_i, \delta_i\}$. M-step maximises the complete data log-likelihood by U_{0i} replaced by corresponding expectation. The EM algorithm provides the best linear unbiased estimates of the individual-specific deviations U_{0i}.

Secondly, based on the estimated values, we can compute measurement error-adjusted estimator based on the linear predictor of the failure-time submodel by

$$\hat{\mathrm{M}}_i = \hat{\gamma}\hat{U}_{0i} \tag{2}$$

where $\hat{U}_{0i}$ is the estimated true deviation of the biomarker value from the population mean at baseline for the ith individual, and $\hat{\gamma}$ is the estimated association parameter between baseline biomarker and hazard for failure. Note that, $\exp(\hat{\gamma})$ is the hazard ratio associated with a unit increase in the value of biomarker at baseline with respect to the population mean. In our simulation study (Section 5), we will extensively explore the validity of $\hat{\mathrm{M}}_i$ as the measurement error-adjusted estimator within time-dependent ROC curve analysis.

4. Estimation of the time-dependent ROC curve at future time horizons

We need to define the *cases* and *controls* at time future time points t_h (>0). Let $R_i(t_h) = I(X_i \geq t_h)$ be at-risk indicator for each individual defining the riskset at a t_h. Then, dichotomise the riskset at time t_h into two mutually exclusive groups: *cases* (experienced failure at time t_h) and *controls* (survived failure beyond time t_h). At any t_h, each diseased individual (i.e. $\delta_i = 1$) plays a role as *control* for an early time $t_h < T_i$ but then play the role of *case* when $t_h = T_i$. In this case, the failure-time is represented through the counting process $N(t_h) = I(T_i \leq t_h)$, and the corresponding increment is defined by $dN(t_h) = N(t_h) - N(t_h -)$ in terms of the failure time T_i alone. This is the incident/dynamic failure-times proposed by Heagerty and Zheng [23] for the estimation of time-dependent ROC curve, and is the version adopted by most methodologists.

Finally, we can assess the discriminatory potential of the measurement error-adjusted estimator $\hat{\mathrm{M}}_i$ at time t_h conditional on a threshold value c. Following the standard ROC curve methodology, $\hat{\mathrm{M}}_i \geq c$ determines the *test* positive (disease presence) and *test* negative (disease absent) if $\hat{\mathrm{M}}_i < c$. The sensitivity and specificity of the error-adjusted baseline estimator at t_h can then be defined by

$$\begin{array}{c} \text{sensitivity}(c,t_h)\text{: } Pr\,\{\hat{\mathrm{M}}_i \geq c|\; dN(t_h) = 1\} \\ \text{specificity}(c,t_h)\text{: } Pr\,\{\hat{\mathrm{M}}_i < c|\; N(t_h) = 0\} \end{array} \tag{3}$$

where $c \in (-\infty, +\infty)$. Sensitivity (c,t_h) estimates the expected fraction of individuals with $\hat{\mathrm{M}}_i \geq c$ among those who experience the failure at t_h, while specificity(c, t_h) estimates the expected fraction of individuals with $\hat{\mathrm{M}}_i < c$ among those who survived failure beyond t_h. To estimate the two conditional probabilities (conditional on incident/dynamic failure-times), we can use the proportional hazards properties of the joint likelihood function related to the failure-time submodel in (1). Xu and O'Quigley [24] proposed estimating the proportion of variation in a covariate that is explained by failure times. They estimated the distribution of the covariate conditional on failure at a time t based on the weights $\pi_k(t)$ from the Cox proportional hazards model. The same approach was later used by Heagerty and Zheng [23] to estimate the time-dependent sensitivities and specificities as defined as (3). Following them, for a given threshold value c, we estimate the sensitivity (or true positive fraction, TPF) at t_h by

$$\text{sensitivity}\,(c,t_h) = Pr\big(\hat{\mathrm{M}}_i \geq c|T_i = t_h\big) = \sum_k I\big(\hat{\mathrm{M}}_k \geq c\big)\,\pi_k(t_h)$$

where $\pi_k(t_h) = R_k(t_h)\exp\big(\hat{\mathrm{M}}_k\big)/W(t_h)$ are the weights under proportional hazards and $W(t_h) = \sum_k R_k(t_h)\exp\big(\hat{\mathrm{M}}_k\big)$ is the total weight for the riskset individuals, and $I(.)$ is an indicator. We can calculate the specificity (or $1 -$ false positive fraction, FPF) empirically by

$$\text{specificity}\,(c,t_h) = P\big(\hat{\mathrm{M}}_i < c|T_i > t_h\big) = \frac{\sum_k I\big(\hat{\mathrm{M}}_k < c\big) R_k^0(t_h)}{\sum_k R_k^0(t_h)}$$

where $R_k^0(t_h)$ is the set of failure-free individuals in the riskset at time t_h and $\sum_k R_k^0(t_h)$ is the size of that control-set.

Bansal and Heagerty [25] have also used the same incident/dynamic failure-times definition when there exists time-specific *cases* of interest at a particular time t_h. However, we apply this definition to estimate the discriminative capability at any time $t_h > 0$ with no such prior information. Note that the proportional hazard assumption does not require any *case* to exist at t_h to estimate the above sensitivity; it will force the FPF equal to zero and specificity equal to one. Thus, although there is no *case* (had a failure) exists at

t_h (which usually happens in practice), sensitivity can still be estimated at t_h. Once the above sensitivity and specificity are computed at t_h, the corresponding time-dependent ROC curve and AUC at time t_h for all $c \in (-\infty, +\infty)$ can be computed by kernel (density) smoothing which follows closely the details of the original data [26]. When there is no specific time t_h of interest, but restricted to a fixed follow-up period $(0,\tau)$, a global summary of the AUC can be provided by a survival concordance index (C-index) [27].

In the proposed approach, $\hat{\mathrm{M}}_i$ is computed from joint model estimates, which is then used as the input to ROC curve analysis; hence, the 95% confidence intervals (CIs) of the AUC, sensitivity and specificity are estimated by the bootstrap sampling with replacement [28] to account for uncertainty due to the two estimation processes. The previously suggested time-dependent ROC models for censored failure-times also used bootstrap approaches to estimate the corresponding CIs [11, 20, 23, 27]. The software to implement the proposed joint model has been developed in R language, and will be available as part of the current `joineR` package [29]. The `risksetROC` package in R can be used to estimate the corresponding incident/dynamic ROC curve [23], and we have modified corresponding R functions to implement the proposed ROC curve. The R codes are available from the authors on request.

5. Simulation investigations

We have conducted three simulation investigations to demonstrate whether the proposed approach is an appropriate framework for estimating the time-dependent ROC curve. The details of data simulation and investigations are given in the supplementary file. Firstly, we explored the accuracy of estimation of association parameter γ from the joint model which is crucial for estimating the correct ROC curve from the proposed approach. For comparison with γ, we also fitted Cox proportional hazard model including the observed baseline biomarker value as a covariate, and also the estimated random intercept terms from the linear mixed effect (LME) model $(\hat{U}_0)_{\mathrm{lme}}$ (usually referred as two-stage model [17]), see more details of these models in supplementary file. Figure 1 presents the bias for estimated association from the proposed joint, observed and $(\hat{U}_0)_{\mathrm{lme}}$ models for 30% censoring. The corresponding numerical values together with mean square error (MSE) and 95% coverage probabilities are given in supplemental table S1, and S2 and S3 present these for 50% and 70% censoring respectively. All estimates were obtained from 500 bootstrap samples with replacement. We observe that the joint model provides the most accurate estimation of the association with smaller biases, lower MSE and coverage probabilities closer to 95% across all settings. Both observed and $(\hat{U}_0)_{\mathrm{lme}}$ approaches underestimate the level of association to a great extent (high bias) when the true association is fairly strong and measurement error is high. The underestimation of the association from the model including observed baseline biomarker value is anticipated, as this approach assumes the biomarker value is measured without error. Although the $(\hat{U}_0)_{\mathrm{lme}}$ approach is computationally simpler than the joint model, due to the two individual regressions it could lead to bias estimation for conditional effects such as the association between the two outcomes. Our observations are also consistent with the previously published simulation study results from various joint model specifications [e.g. 17, 20]. The proposed joint model estimates the association fairly close to the true value with lower bias even when the measurement error is high; indicating that the proposed model makes the proper adjustment of measurement error when estimating the underlying association at the baseline level, and strengthening the case of using the model for estimating association between biomarker and risk of failure at baseline.

[insert Figure 1.]

Secondly, we evaluated how the proposed measurement error-adjusted estimator $\hat{\mathrm{M}}$ modifies the ROC curve on a given association γ. The C-index of $\hat{\mathrm{M}}$ for a fixed follow-up period of (0, 2) was computed for varying level of association and compared with the true C-index (based on the true biomarker value at baseline). To compare with the proposed estimator, we used the observed baseline value, as the observed baseline value is generally used in ROC curve analyses. And due to computational simplicity of $(\hat{U}_0)_{\mathrm{lme}}$, we also considered it as a potential estimator for the time-dependent ROC curve analysis, but $(\hat{U}_0)_{\text{lme}}$ has not been previously used as an estimator of its own for the time-dependent ROC curve [11]. Figure 2 presents the estimated C-Indexes for 30% censoring for various strengths of association. The corresponding numerical values together with bias, MSE and 95% coverage probabilities are given in supplemental table S4, and S5 and S6 present these for 50% and 70% censoring respectively. When there is no association between the baseline biomarker and failure, the C-index is estimated from the proposed estimator $\hat{\text{M}}$ fairly close to the null value of 0.5 (indicating that biomarker shows no discriminatory potential) across all settings of γ and censoring %s, see supplemental tables. As strength of the association is stronger (γ moves towards 1.0), the estimated C-index from $\hat{\text{M}}$ is also increased by acceptable margins. We can observe from Figure 2 that the point estimate of the C-Index from both $\hat{\text{M}}$ and $(\hat{U}_0)_{\text{lme}}$ are fairly similar, especially when the association is weak to moderate, and $(\hat{U}_0)_{\text{lme}}$ point estimate is better as compared to the observed value. However, $(\hat{U}_0)_{\text{lme}}$ substantially under-coverage the 95% confidence intervals as compared to that from $\hat{\text{M}}$, especially when the association is moderate to strong; see Supplementary tables S4, S5, and S6. The coverage issue associated with $(\hat{U}_0)_{\text{lme}}$ is also observed in association estimation (supplementary tables S1, S2, and S3). Therefore, we can expect the same extent of under-coverage for other ROC curve summaries, implying $(\hat{U}_0)_{\text{lme}}$ is failed as an estimator for the time-dependent ROC curve analysis. $\hat{\text{M}}$ provides the most accurate C-index estimation with smaller biases, and also with lower MSE and higher 95% coverage probabilities across all settings of γ and censoring %s.

[insert Figure 2.]

Finally, the accuracy of the time-dependent ROC curve was further evaluated by comparing the estimated $\text{AUC}(t_h)$ at future time points t_h with the true $\text{AUC}(t_h)$. We also computed the $\text{sensitivity}(t_h)$ and $\text{specificity}(t_h)$ at optimal thresholds for the proposed $\hat{\text{M}}$, and compared with the observed baseline value estimates. Table 1 presents the bias for estimated $\text{AUC}(t_h)$ at $t = t_h = 1, 2, 3, 4$ for $\gamma = 1$ and 30% censoring and estimated $\text{sensitivity}(t_h)$ and $\text{specificity}(t_h)$. Supplemental table S7 to S21 present bias, MSE and 95% coverage probabilities of estimates for all values of γ and censoring rates. The estimated $\text{AUC}(t_h)$ from the proposed measurement error-adjusted $\hat{\text{M}}$ is more accurate, with lower biases and MSE as compared to the observed baseline value. We observe that $\hat{\text{M}}$ is failed to archive the nominal coverage when the measurement error is considerably high at early time points; however, such high measurement error is rarely observed in current clinical data due to precision of latest machinery and better laboratory regulations. This investigation proves that the proposed methodology effectively corrected for a moderate measurement error when calculating performance of the baseline biomarker at future time points. As expected, $\text{AUC}(t_h)$ decreases as t_h increases because discriminatory potential of the biomarker becomes weaker as departing from baseline [23].

Table 1: Time-dependent AUC (Standard Error, SE) and Bias at t_h for the measurement-error adjusted and observed biomarker when $\gamma = 1$ and 30% censoring for varying measurement error variance. Sensitivity (SE) and specificity (SE) are estimated at the corresponding optimal threshold.

t_h	Measurement-error Adjusted				Observed baseline value			
	AUC(SE)	Bias	Sensitivity (SE)	Specificity(SE)	AUC(SE)	Bias	Sensitivity(SE)	Specificity(SE)
Measurement error $\sigma_e^2 = 0.25$								
1	0.73(0.02)	-0.02	0.67 (0.01)	0.66 (0.01)	0.70(0.02)	-0.04	0.65 (0.01)	0.65 (0.01)
2	0.70(0.01)	-0.02	0.65 (0.01)	0.64 (0.01)	0.69(0.01)	-0.03	0.64 (0.01)	0.64 (0.01)
3	0.68(0.01)	-0.02	0.64 (0.01)	0.63 (0.01)	0.68(0.01)	-0.02	0.63 (0.01)	0.62 (0.01)
4	0.66(0.02)	-0.02	0.62 (0.02)	0.61 (0.02)	0.66(0.02)	-0.02	0.62 (0.02)	0.61 (0.02)
Measurement error $\sigma_e^2 = 0.5$								
1	0.72(0.02)	-0.03	0.66 (0.01)	0.66 (0.01)	0.68(0.02)	-0.06	0.63 (0.01)	0.63 (0.01)
2	0.70(0.02)	-0.03	0.65 (0.01)	0.64 (0.01)	0.67(0.01)	-0.05	0.62 (0.01)	0.62 (0.01)
3	0.67(0.01)	-0.03	0.63 (0.01)	0.62 (0.01)	0.66(0.01)	-0.04	0.62 (0.01)	0.61 (0.01)

4	0.65(0.02)	-0.03	0.61 (0.02)	0.60 (0.02)	0.65(0.02)	-0.03	0.61 (0.02)	0.60 (0.02)
Measurement error $\sigma_e^2 =$ 1.0								
1	0.71(0.02)	-0.04	0.65 (0.02)	0.65 (0.01)	0.65(0.02)	-0.09	0.61 (0.01)	0.61 (0.01)
2	0.69(0.02)	-0.04	0.64 (0.01)	0.63 (0.01)	0.64(0.01)	-0.08	0.60 (0.01)	0.60 (0.01)
3	0.66(0.01)	-0.04	0.62 (0.01)	0.61 (0.01)	0.64(0.01)	-0.06	0.60 (0.01)	0.60 (0.01)
4	0.64(0.02)	-0.04	0.61 (0.02)	0.59 (0.02)	0.63(0.02)	-0.05	0.59 (0.02)	0.59 (0.02)
Measurement error $\sigma_e^2 =$ 1.5								
1	0.70(0.02)	-0.04	0.65 (0.02)	0.64 (0.02)	0.63(0.02)	-0.11	0.59 (0.01)	0.59 (0.01)
2	0.68(0.02)	-0.04	0.64 (0.02)	0.63 (0.01)	0.63(0.01)	-0.10	0.59 (0.01)	0.59 (0.01)
3	0.66(0.02)	-0.04	0.62 (0.01)	0.61 (0.01)	0.62(0.01)	-0.08	0.59 (0.01)	0.59 (0.01)
4	0.63(0.02)	-0.04	0.60 (0.02)	0.59 (0.02)	0.62(0.02)	-0.06	0.58 (0.01)	0.58 (0.02)
Measurement error $\sigma_e^2 =$ 2.0								
1	0.69(0.02)	-0.05	0.64 (0.02)	0.64 (0.02)	0.62(0.02)	-0.13	0.58 (0.01)	0.58 (0.01)
2	0.68(0.02)	-0.05	0.63 (0.02)	0.62 (0.01)	0.62(0.01)	-0.11	0.58 (0.01)	0.58 (0.01)
3	0.65(0.02)	-0.05	0.62 (0.01)	0.61 (0.01)	0.61(0.01)	-0.09	0.58 (0.01)	0.58 (0.01)
4	0.63(0.02)	-0.05	0.60 (0.02)	0.59 (0.02)	0.59(0.02)	-0.07	0.58 (0.01)	0.57 (0.02)
Measurement error $\sigma_e^2 =$ 2.5								
1	0.70(0.02)	-0.06	0.64 (0.02)	0.63 (0.02)	0.61(0.02)	-0.14	0.58 (0.01)	0.58 (0.01)
2	0.67(0.02)	-0.05	0.63 (0.02)	0.62 (0.01)	0.61(0.01)	-0.12	0.58 (0.01)	0.57 (0.01)
3	0.65(0.01)	-0.05	0.62 (0.02)	0.60 (0.01)	0.60(0.01)	-0.10	0.57 (0.01)	0.57 (0.01)
4	0.63(0.02)	-0.05	0.60 (0.02)	0.58 (0.02)	0.60(0.02)	-0.08	0.57 (0.01)	0.57 (0.01)

6. Application: Mayo Clinic primary biliary cirrhosis (PBC) study

We apply the proposed approach to the data from the Mayo Clinic trial in primary biliary cirrhosis (PBC) of the liver conducted between 1974 and 1984. PBC is a fatal, but rare liver disease. If PBC is not treated, and reaches an advanced stage, it can lead to several major complications, including death. The trial randomised 312 patients between D-penicillamine (n = 158) for the treatment of PBC and placebo (n = 154) [30]. Among the 312 patients randomised, 125 died during the follow-up. Although the study established that D-penicillamine is not effective for the treatment of PBC, the data have been used to develop clinical prediction models, and has been widely analysed using joint modelling methods [31,32,33,34]. Patients with PBC typically have abnormalities in several blood tests; hence, during the study follow-up several biomarkers associated with liver function were serially recorded for these patients. In this article, we considered three biomarkers: serum bilirubin (measured in units of mg/dl), serum albumin (mg/dl), and prothrombin time (seconds) with the aim of assessing the performance of each biomarker at the baseline level for patient survival. The available longitudinal measurements of each biomarker were used to correct for measurement error. As the proposed modelling framework assumes Gaussian random effects and errors, the bilirubin measurements were log-transformed and the prothrombin time were transformed by $(0.1 \times \text{prothrombin time})^{-4}$ as suggested by Box-Cox transformation. Albumin did not require transformation. A linear trajectory is assumed for each biomarker and the residual plots did not indicate any deviations from the linear form; see supplementary file for diagnostic plots.

Table 2 shows the estimated time-dependent AUC, sensitivity and specificity at times $t_h =$ Year 1, Year 5 and Year 10 together with estimated measurement error and association parameter for both the measurement error-adjusted and observed baseline biomarker. The 95% confidence intervals (CI) were computed from 500 bootstrap samples with replacement. The measurement error-adjusted estimator is associated with a considerably high time-dependent AUC(t_h) than the observed baseline biomarker at all t_h, and this is observed across all three biomarkers. The level of association between the baseline biomarker and risk of death is also substantially underestimated as the measurement error is ignored. Among the three biomarkers, once corrected for the measurement error, the highest time-dependent AUC(t_h) was achieved for serum bilirubin, which means that among the 3 biomarkers, serum bilirubin is best for the earliest diagnosis of PBC. The ROC(t_h) curves at three discrete time points and time-dependant AUC(t_h) over continuous time for serum bilirubin are shown in Figure 3.

Table 2: Time-dependent AUC, sensitivity and specificity (at the corresponding optimal threshold) at t_h for the measurement-error adjusted and observed baseline biomarkers

Biomarker ($\hat{\sigma}_e^2$)	t_h	Measurement-error Adjusted (95% CI)				Observed value (95% CI)			
		Association	AUC	Sensitivity	Specificity	Association	AUC	Sensitivity	Specificity
Bilirubin $\hat{\sigma}_e^2 =$ 0.12 95% CI (0.10, 0.14)	Year 1	1.34 (1.20, 1.72)	0.85 (0.79, 0.88)	0.79 (0.72, 0.84)	0.78 (0.70, 0.78)	1.06 (0.92, 1.28)	0.80 (0.75, 0.83)	0.73 (0.68, 0.78)	0.72 (0.68, 0.76)
	Year 5		0.79 (0.73, 0.81)	0.67 (0.61, 0.72)	0.78 (0.69, 0.79)		0.74 (0.70, 0.77)	0.62 (0.57, 0.68)	0.74 (0.69, 0.78)
	Year 10		0.67 (0.64, 0.72)	0.61 (0.52, 0.72)	0.67 (0.55, 0.72)		0.66 (0.60, 0.70)	0.59 (0.48, 0.64)	0.65 (0.57, 0.75)
Prothrombin Time $\hat{\sigma}_e^2 =$ 0.03 95% CI (0.02, 0.03)	Year 1	-6.39 (-7.98, -4.96)	0.78 (0.72, 0.82)	0.72 (0.66, 0.76)	0.71 (0.65, 0.74)	-3.33 (-4.37, -2.47)	0.70 (0.65, 0.74)	0.67 (0.60, 0.73)	0.63 (0.57, 0.66)
	Year 5		0.74 (0.70, 0.77)	0.73 (0.68, 0.76)	0.63 (0.58, 0.68)		0.70 (0.64, 0.73)	0.73 (0.57, 0.74)	0.55 (0.51, 0.70)
	Year 10		0.71 (0.66, 0.74)	0.70 (0.61, 0.77)	0.61 (0.50, 0.69)		0.65 (0.60, 0.69)	0.59 (0.45, 0.65)	0.63 (0.53, 0.74)
Albumin $\hat{\sigma}_e^2 =$ 0.11 95% CI (0.10, 0.13)	Year 1	-4.72 (-6.42, -3.77)	0.82 (0.77,0.86)	0.77 (0.71, 0.81)	0.71 (0.66, 0.79)	-1.67 (-2.32, -1.42)	0.69 (0.64, 0.73)	0.59 (0.55, 0.66)	0.67 (0.61, 0.73)
	Year 5		0.77 (0.73, 0.80)	0.70 (0.64, 0.76)	0.71 (0.67, 0.75)		0.66 (0.63, 0.70)	0.58 (0.54, 0.63)	0.65 (0.58, 0.70)
	Year 10		0.65 (0.61, 0.70)	0.65 (0.48, 0.73)	0.57 (0.49, 0.70)		0.62 (0.58, 0.65)	0.70 (0.59, 0.75)	0.47 (0.42, 0.60)

[insert Figure 3.]

7. Discussion

The focus of this article was to develop a novel methodology for evaluating time dependent performance of the baseline biomarker correcting for measurement error. We proposed a novel utility of the joint modelling framework within the theory of time-dependent ROC curve analysis by developing a more efficient estimator that links the risk of failure and baseline biomarker. The baseline is an important time point as the biomarker value at baseline can serve as the earliest indicator of a potential future adverse clinical event (e.g. death). We have shown from our simulation investigations that measurement error could cause a severe bias in estimating the association between the baseline biomarker and risk of failure event. Although, this has been investigated in joint modelling literature in relation to various specifications of the model, this study was the first to show that observed baseline value could severely underestimate the true discriminative capability of the biomarker as estimated by AUC. Our simulation investigations proved that the proposed methodology effectively corrects for a moderate measurement error when calculating the performance of the baseline biomarker over time.

A similar joint model specification was suggested by Crowther et al. [35] to predict survival for new patients. In their model, association was defined on the current biomarker value rather than the individual-level deviation, and restricted cubic splines were used to define the longitudinal biomarker while failure-time assumes a parametric distribution. This level of complexity is necessary to model highly nonlinear biomarker trajectories over time, and to capture complex baseline hazards when predicting the future survival probabilities. However, our aim was to quantify the true discriminant capability of the baseline biomarker at future time points, and a more classical modelling and estimation framework has been proven sufficient from our thorough simulation study. To facilitate the use of the methods in practice, software is written in R language (which is a free software environment). The proposed approach can be implemented with a relatively low computational burden; for example, in our application dataset with 312 patients, the proposed joint model for each biomarker took under 1 minutes to converge on a standard desktop computer, and the time-dependent AUCs were derived in few seconds.

More recently, quantities such as proportion of information gain (PIG) have been proposed to measure the importance of a biomarker. Li and Qu [36] adjusted for the measurement error in calculating the PIG for continuous, binary and failure-time outcomes. However, our focus in this article was to account for the measurement error of a more familiar and well established quantity among the medical research community. We proposed a computationally simple approach to estimate the true time-dependent ROC curve for a baseline biomarker subjected to measurement error. Although information from longitudinally repeated measurements is required for the proposed approach in addition to the single biomarker measurement at baseline, often in clinical studies, longitudinal measurements are recorded alongside the main study as secondary outcomes, e.g. to monitor the progression of a disease. Therefore, the prospects of utilising the proposed framework to detect the true performance of biomarkers is quite substantial.

The proposed ROC curve approach can be extended to incorporate multiple biomarkers by utilising multivariate joint models (e.g. Hickey et al. [34]). In our application, we evaluated the measurement error-corrected performance of three biomarkers in separation for the survival of PBC patients. It may be of interest to assess the performance in a combination of biomarkers, as in many diseases it is unlikely that a single biomarker will ever be more effective due to complexity of the disease (e.g. Aerts et al. [37]).

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest.

References

1. Adams LA. Biomarkers of liver fibrosis. J. Gastroen Hepatol. 2011; 26(5): 802-809.
2. Toh CH, Ticknor LO, Downey C, Giles AR, Paton R, Wenstone R. Early identification of sepsis and mortality risks through simple, rapid clot-waveform analysis. Intens. Care Med. 2003; 29: 55-61.
3. Keogh RH, White IR. A toolkit for measurement error correction, with a focus on nutritional epidemiology. Stat Med. 2014; 33 (12): 2137-2155.
4. Tsiatis AA, Degruttola V, Wulfsohn MS. Modeling the relationship of survival to longitudinal data measured with error. Applications to survival and CD4 counts in patients with AIDS. J. Am. Stat. Assoc. 1995; 90: 27–37.
5. Wulfsohn MS, Tsiatis AA. A joint model for survival and longitudinal data measured with error. Biometrics. 1997; 53: 330–339.
6. Zweig MH, Campbell G. Receiver-operator characteristic plots: A fundamental evaluation tool in clinical medicine. Clin. Chem. 1993; 39: 561–577.
7. Cai T, Pepe MS, Zheng Y, Lumley T, Jenny NS. The sensitivity and specificity of markers for event times. Biostatistics. 2006; 7(2): 182–197.
8. George J, Claes P, Vunckx K, Tejpar S, Deroose C, Nuyts J, Loeckx D, Suetens, P. A textural feature based tumor therapy response prediction model for longitudinal evaluation with PET imaging. 2012 9th IEEE International Symposium on Biomedical Imaging (ISBI). 2012; 1048-1051.
9. Lu Y, Wang L, Liu P, Yang P, You M. Gene-expression signature predicts postoperative recurrence in stage I non-small cell lung cancer patients. PLoS One. 2012; 7(1): e30880.
10. Chen H, Zhang Y, Li S, Li N, Chen Y, Zhang B. et al. Direct comparison of five serum biomarkers in early diagnosis of hepatocellular carcinoma. Cancer Manage. Res. 2018; 10:1947–1958.
11. Kamarudin AN, Cox T, Kolamunnage-Dona R. Time-dependent ROC curve analysis in medical research: current methods and applications. BMC Med Res Methodol. 2017;17:53. DOI: 10.1186/s12874-017-0332-6
12. Faraggi D. The effect of random measurement error on receiver operating characteristic (ROC) curves. Statist. Med. 2000; 19: 61–70.
13. Reiser B. Measuring the effectiveness of diagnostic markers in the presence of measurement error through the use of ROC curves. Statist. Med. 2000; 19: 2115–2129.
14. Henderson R, Diggle P, Dobson A. Joint modelling of longitudinal measurements and event time data. Biostatistics. 2000; 1: 465-480.
15. Gould AL, Boye ME, Crowther MJ, Ibrahim JG, Quartey G, Micallef S, Bois FY. Joint modeling of survival and longitudinal non-survival data: current methods and issues. Report of the DIA Bayesian joint modeling working group. Statist. Med. 2015;34(14):2181-2195.
16. Tsiatis A, Davidian M. Joint modeling of longitudinal and time-to-event data: an overview. Statistica Sinica. 2004; 14: 809–34.
17. Sweeting MJ, Thompson SG. Joint modelling of longitudinal and time-to-event data with application to predicting abdominal aortic aneurysm growth and rupture. Biom. J. 2011; 53(5): 750 – 763.
18. Proust-Lima C, Taylor JM. Development and validation of a dynamic prognostic tool for prostate cancer recurrence using repeated measures of posttreatment PSA: a joint modeling approach. Biostatistics. 2009; 10(3): 535-549.
19. Garre F, Zwinderman A, Geskus R, Sijpkens Y. A joint latent class changepoint model to improve the prediction of time to graft failure. Journal of the Royal Statistical Society, Series A, 2008; 171, 299–308.
20. Kolamunnage-Dona R, Williamson PR. Time-dependent efficacy of longitudinal biomarker for clinical endpoint. Stat Methods Med Res. 2016; 27(6): 1909–1924. (Article first published online: October 17, 2016; Issue published: June 1, 2018).

21. Rizopoulos, D. Dynamic predictions and prospective accuracy in joint models for longitudinal and time-to-event data. Biometrics. 2011; 67(3): 819-829.
22. Henderson R, Diggle P, Dobson A. Identification and efficacy of longitudinal markers for survival. Biostatistics. 2002; 3(1): 33-50.
23. Heagerty PJ, Zheng Y. Survival Model Predictive Accuracy and ROC curves. Biometrics. 2005; 61: 92 – 105.
24. Xu R, O'Quigley J. Proportional hazards estimate of the conditional survival function. J R Stat Soc Series B. 2000; 62(4):667-680.
25. Bansal A, Heagerty PJ: A tutorial on evaluating time-varying discrimination accuracy for survival models used in dynamic decision-making. Med Decis Making. 2018; 38(1). DOI: 10.1177/0272989X18801312.
26. Zou KH, Hall WJ, Shapiro DE. Smooth non-parametric receiver operating characteristic (ROC) curves for continuous diagnostic tests. Stat Med. 1997; 16:2143–2156.
27. Heagerty PJ, Lumley T, Pepe MS. Time dependent ROC curves for censored survival data and a diagnostic marker. Biometrics. 2000; 56:337-344.
28. Efron B, Tibshirani RJ. An introduction to the bootstrap. New York: Chapman and Hall.1993.
29. Philipson P, Diggle P, Sousa I, Kolamunnage-Dona R, Williamson P, Henderson R. joineR: Joint modelling of repeated measurements and time-to-event data. 2012. Comprehensive R Archive Network, United Kingdom
30. Fleming TR, Harrington DP. Counting processes and survival analysis. New Jersey: John Wiley & Sons; 2011.
31. Andrinopoulou E-R, Rizopoulos D. Bayesian shrinkage approach for a joint model of longitudinal and survival outcomes assuming different association structures. Stat Med. 2016; 35(26):4813–23.
32. Albert PS, Shih JH. An approach for jointly modeling multivariate longitudinal measurements and discrete time-to-event data. Ann Appl Stat. 2010; 4(3):1517–32.
33. Crowther MJ, Abrams KR, Lambert PC. Joint modeling of longitudinal and survival data. Stata J. 2013;13(1):165–84.
34. Hickey G, Philipson P, Jorgensen A, Kolamunnage-Dona R. joineRML: A joint model and software package for time-to-event and multivariate longitudinal outcomes. BMC Med Res Methodol. 2018; 18:50.
35. Crowther MJ, Lambert PC, Abrams KR. Adjusting for measurement error in baseline prognostic biomarkers included in a time-to-event analysis: a joint modelling approach. BMC Med Res Methodol. 2013; 13(1):146.
36. Li W, Qu Y. Adjustment for the measurement error in evaluating biomarkers. Stat Med. 2010; 29(22): 2338-46.
37. Aerts M., Benteyn D., Van Vlierberghe H., Thielemans K. and Reynaert H. Current status and perspectives of immune-based therapies for hepatocellular carcinoma. World J. Gastroenterol. 2016; 22, 253–261

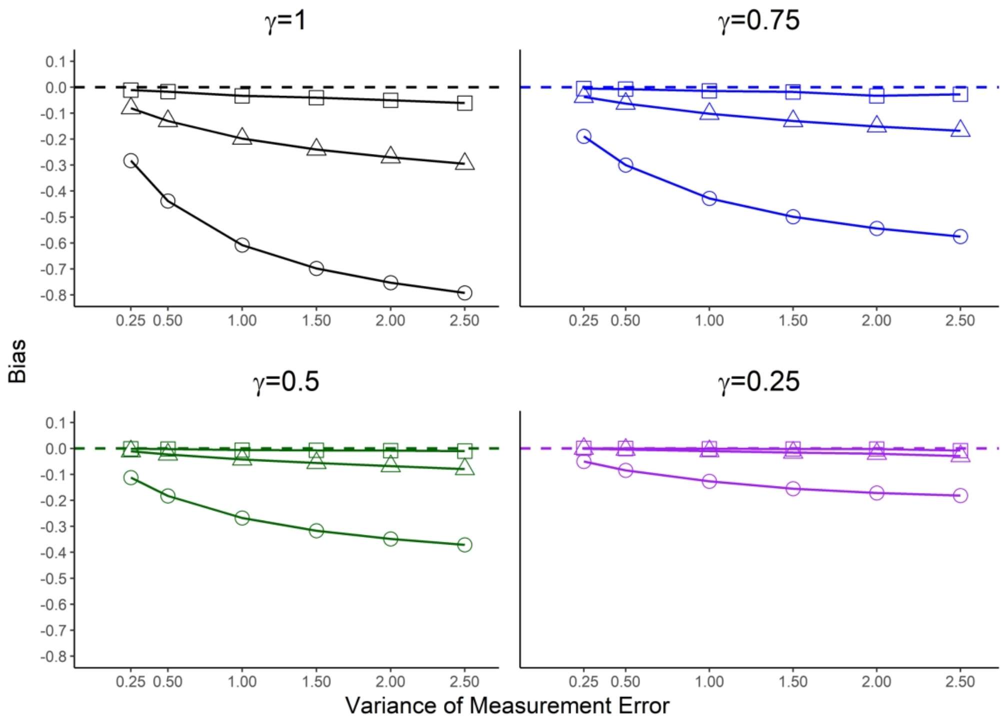

Figure 1. Bias for estimated association when censoring is 30%. Square indicates the estimated association from the proposed joint model, circle the Cox model with observed baseline value and triangle the estimated random intercept term from the LME model. The horizontal dashed line indicates no bias.

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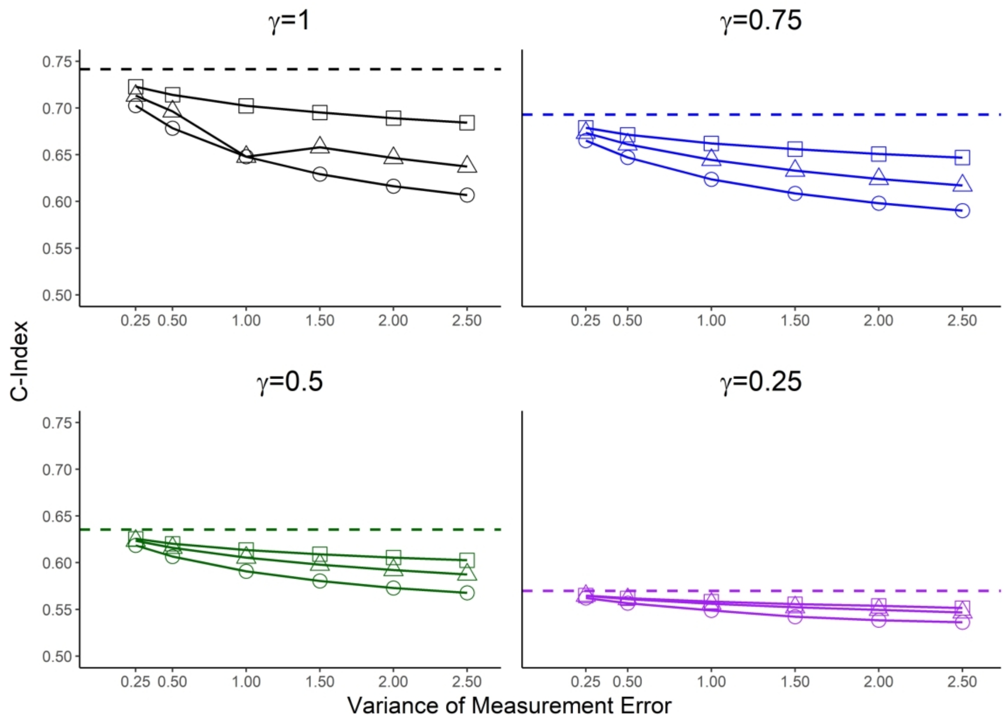

Figure 2. Estimated C-Index for 30% censoring. Square indicates the estimated value from the proposed measurement adjusted model, circle the Cox model with observed baseline value and triangle the estimated random intercept term from the LME model. The horizontal dashed line is the true C-index for corresponding association parameter.

228x165mm (300 x 300 DPI)

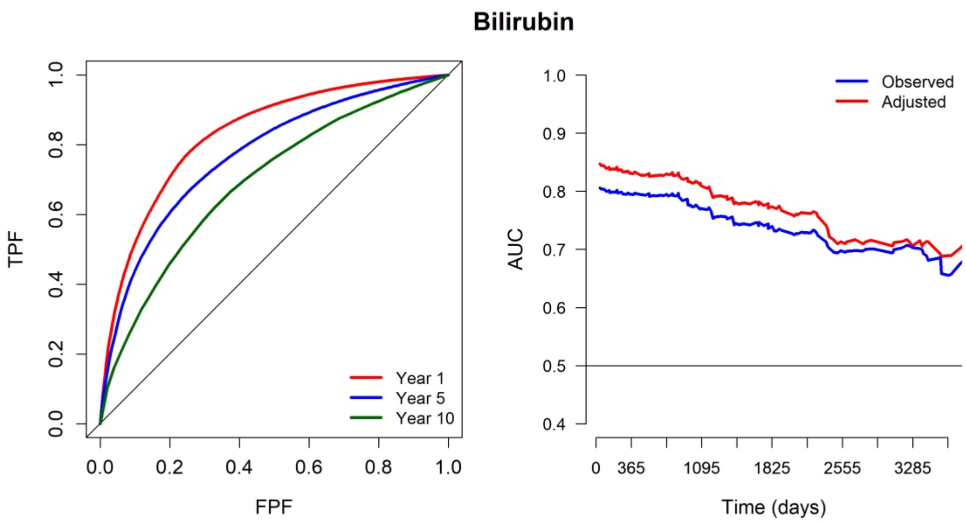

Figure 3. PBC data – ROC(t) curves (left) and time dependent AUC over the progression of time (right) for serum bilirubin

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Supplemental material for "Adjustment for the measurement error in evaluating biomarker performances at baseline for future survival outcomes: Time dependent ROC curve within a joint modelling framework"

Data simulation and investigations

The longitudinal values of a biomarker (y_i) were simulated for 500 individuals ($i = 1, ..., 500$) under a linear mixed model with fixed (population-level) intercept and slope with coefficients $\beta_0 = 1$ and $\beta_1 = -1$ respectively, and random intercept U_0 and random slope U_1 terms, and measurement error ε_{ij} using $y_i(t_{ij}) = 1 - t_{ij} + U_{0i} + U_{1i}t_{ij} + \varepsilon_{ij}$. The corresponding true values were simulated without the term ε_{ij} by $Y_i(t_{ij}) = 1 - t_{ij} + U_{0i} + U_{1i}t_{ij}$ at times t_{ij}. Longitudinal times t_{ij} were set at 0, 1, 2, 3, 4, 5, so a maximum of 6 longitudinal observations recorded at these time points up to individual's failure time in the final dataset. The U_0 and U_1 were generated from the bivariate normal distribution $N(0,\Sigma_U)$ with variances 1 and covariance 0.5, and measurement error ε_{ij} was generated from $N(0,\sigma_e^2)$. The true (without measurement error) and observed (with measurement error) values at baseline are extracted from the simulated longitudinal datasets at time $t_{ij} = 0$. We varied $\sigma_e^2 =$ 0.25, 0.5, 1.0, 1.5, 2.0 and 2.5 to allow low to substantially high measurement error in biomarker values in order to assess the impact of measurement error on the proposed approach.

Failure times T_i were generated under Gompertz distribution with scale parameter θ_0 and shape parameter θ_1 assuming Cox proportional hazards model $\lambda_i(t) = \lambda_{0i}(t)\exp(\gamma U_{0i})$ (see Bender et al. [1] for more details) by

$$T_i = \frac{1}{\theta_{1i}}\log\left\{1 - \frac{\theta_{1i}\log(X_i)}{\lambda_i}\right\}$$

where X_i is derived from the uniform[0,1] distribution, and $\lambda_i = \exp(\theta_0 + \gamma U_{0i})$. We set $\theta_0 =$ -3 and $\theta_1 =$ 1. An exponential distribution parameters were used to control the censoring rate. We varied $\gamma = \{0.25, 0.50, 0.75, 1\}$ to allow weak (0.25) to strong (1) association between the baseline biomarker value and failure times. The censoring rate was varied approximately at 70%, 50% and 30% by setting the exponential distribution parameter at $\exp(-2)$, $\exp(-1.3)$ and $\exp(-0.6)$ respectively. We examined only positive associations ($\gamma > 0$), however, the behaviour for negative associations with the same strength would be the same, but in opposite direction, and will not impact on biases and other characteristics.

Investigation 1: We explored the accuracy of estimation of association parameter γ from the joint model which is crucial for estimating the correct ROC summaries from the proposed approach. We compare the proposed joint modelling estimation of the association between the baseline biomarker and failure with two standard approaches;

(1) Cox proportional hazards model including the observed biomarker value y_{i0} at baseline as a covariate, i.e. $\lambda_i(t) = \lambda_0(t)\exp\{\alpha y_{i0}\}$.
    The Cox regression parameter α estimates the association between risk of the failure and baseline value of the biomarker; hence α is comparable to γ in the proposed joint modelling formulation.

(2) Two-stage model: in the first stage, linear mixed effect (LME) model is fitted to the longitudinal data y_{ij} and in the second stage the estimated random intercept term from the LME model $(\hat{U}_{0i})_{\text{lme}}$ is included as a covariate in the Cox model, so $\lambda_i(t) = \lambda_0(t)\exp\{\alpha(\hat{U}_{0i})_{\text{lme}}\}$.
The parameter α estimates the corresponding association, and comparable to γ in the proposed joint modelling formulation.

The estimates of association were evaluated by bias, mean square error (MSE) and coverage compared to the true value of γ. The *survival* and *nlme* packages in R were used to fit the Cox and LME models respectively. The estimates were based on 500 independent samples.

Investigation 2: We evaluated how the proposed measurement error-adjusted estimator $\hat{\text{M}}$ modifies the ROC curve on association γ. The C-index of $\hat{\text{M}}$ for a fixed follow-up period of (0, 2) was computed for varying level of association and compared with the true C-index (based on the true biomarker value at baseline Y_0). To explore further, we also estimated C-index of the same fixed follow-up period (0, 2) for the observed y_0 and the LME random intercept estimate $(\hat{U}_0)_{\text{lme}}$. The estimated C-index were evaluated by bias, MSE and coverage with respect to the true C-index. We have used *risksetROC* package in R to compute the C-index for true, observed and LME random intercept values. The C-index of $\hat{\text{M}}$ was derived from our modified R functions. The estimates were based on 500 independent samples.

Investigation 3: The accuracy of the time-dependent ROC curve was further evaluated by comparing the estimated AUC(t_h) at $t_h = 1, 2, 3, 4$ with the true AUC(t_h). The true AUC(t_h) was estimated from the true baseline biomarker value. We also computed the sensitivity(t_h) and specificity(t_h) at optimal thresholds for the proposed $\hat{\text{M}}$. The estimated AUC(t_h) were evaluated by bias, MSE and coverage with respect to the true AUC(t_h) at each t_h, and compared further with the same ROC curve summaries estimated from the observed baseline value y_0. The estimates are based on 500 independent samples.

1. Bender R, Augustin T, Blettner M. Generating survival times to simulate Cox proportional hazards models. Statist. Med. 2005; 24: 1713-1723.

Simulation results

SE – standard error; MSE – mean square error; Bias = True value - Estimated value; Cov – 95% coverage probability

Table S1: Association parameters for varying measurement error with 30% censoring

True γ	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.25															
0	-0.00	0.0569	0.003	-0.0025	94.2	0.00	0.0605	0.0037	-0.0018	95.0	0.00	0.0713	0.0051	-0.0025	94.2
0.25	0.25	0.0602	0.004	-0.0017	94.6	0.20	0.0551	0.0059	-0.0531	84.2	0.25	0.0668	0.0045	-0.0027	94.8
0.50	0.50	0.0684	0.005	-0.0037	94.8	0.39	0.0575	0.0161	-0.1131	50.2	0.49	0.0699	0.0050	-0.0124	94.6
0.75	0.74	0.0774	0.006	-0.0086	95.4	0.56	0.0624	0.0387	-0.1866	16.4	0.71	0.0755	0.0070	-0.0364	90.2
1	0.99	0.0876	0.008	-0.0162	95.2	0.72	0.0705	0.0810	-0.2757	3.2	0.92	0.0835	0.0129	-0.0769	83.6

True γ	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.5															
0	-0.00	0.0598	0.008	-0.0027	94.6	0.00	0.0550	0.0030	-0.0015	94.6	0.00	0.0732	0.0054	-0.0026	94.6
0.25	0.25	0.0642	0.005	-0.0023	94.8	0.16	0.0499	0.0101	-0.0872	56.2	0.24	0.0696	0.0049	-0.0060	94.6
0.50	0.50	0.0748	0.006	-0.0059	95.2	0.32	0.0521	0.0367	-0.1844	6.4	0.48	0.0733	0.0060	-0.0241	93.6
0.75	0.74	0.0872	0.008	-0.0138	93.4	0.45	0.0564	0.0921	-0.2982	0.0	0.69	0.0795	0.0104	-0.0641	85.4
1	0.98	0.1010	0.011	-0.0264	94.6	0.57	0.0631	0.1884	-0.4295	0.0	0.87	0.0871	0.0239	-0.1277	67.6
Measurement error $\sigma_e^2 =$ 1.0															
0	-0.00	0.0636	0.004	-0.0028	94.4	0.00	0.0472	0.0022	-0.0011	95.0	0.00	0.0754	0.0057	-0.0027	94.4
0.25	0.25	0.0698	0.005	-0.0034	95.4	0.12	0.0431	0.0185	-0.1292	15.8	0.24	0.0737	0.0056	-0.0126	93.4
0.50	0.49	0.0829	0.007	-0.0089	95.2	0.23	0.0449	0.0745	-0.2693	0.0	0.46	0.0788	0.0081	-0.0435	90.8
0.75	0.74	0.1006	0.010	-0.0200	95.2	0.32	0.0480	0.1837	-0.4260	0.0	0.65	0.0866	0.0182	-0.1035	77.8
1	0.97	0.1223	0.016	-0.0386	95.4	0.40	0.0530	0.3601	-0.5977	0.0	0.81	0.0938	0.0462	-0.1933	43.6
Measurement error $\sigma_e^2 =$ 1.5															
0	-0.00	0.0662	0.004	-0.0028	94.2	0.00	0.0420	0.0018	-0.0008	94.8	0.00	0.0768	0.0059	-0.0027	94.6
0.25	0.25	0.0717	0.005	-0.0041	94.4	0.10	0.0386	0.0252	-0.1540	2.0	0.23	0.0768	0.0062	-0.0184	93.0
0.50	0.49	0.0913	0.008	-0.0110	95.2	0.18	0.0401	0.1029	-0.3183	0.0	0.44	0.0832	0.0104	-0.0587	88.8
0.75	0.73	0.1119	0.013	-0.0236	94.4	0.25	0.0425	0.2491	-0.4973	0.0	0.62	0.0929	0.0259	-0.1314	69.6
1	0.96	0.1469	0.023	-0.0486	94.0	0.31	0.0463	0.4759	-0.6883	0.0	0.76	0.1002	0.0660	-0.2366	32.8
Measurement error $\sigma_e^2 =$ 2.0															
0	-0.00	0.0682	0.005	-0.0028	95.0	0.00	0.0381	0.0015	-0.0007	94.8	0.00	0.0779	0.0061	-0.0026	94.4
0.25	0.25	0.0760	0.006	-0.0047	94.4	0.08	0.0353	0.0303	-0.1703	0.2	0.23	0.0794	0.0068	-0.0233	92.4
0.50	0.49	0.0980	0.010	-0.0136	95.2	0.15	0.0365	0.1239	-0.3501	0.0	0.43	0.0870	0.0126	-0.0711	86.4
0.75	0.72	0.1719	0.031	-0.0209	95.4	0.21	0.0380	0.2914	-0.5385	0.0	0.60	0.1042	0.0323	-0.1464	70.2
1	0.95	0.1602	0.028	-0.0433	94.0	0.26	0.0397	0.5533	-0.7428	0.0	0.74	0.1156	0.0799	-0.2579	33.0
Measurement error $\sigma_e^2 =$ 2.5															
0	-0.00	0.0700	0.005	-0.0028	94.6	0.00	0.0352	0.0012	-0.0006	94.2	0.00	0.0791	0.0063	-0.0025	94.8
0.25	0.24	0.0825	0.007	-0.0052	94.6	0.07	0.0328	0.0342	-0.1820	0.0	0.22	0.0816	0.0074	-0.0274	92.6
0.50	0.49	0.1044	0.011	-0.0161	94.8	0.13	0.0338	0.1399	-0.3724	0.0	0.42	0.0907	0.0149	-0.0813	84.4
0.75	0.72	0.1311	0.018	-0.0300	94.8	0.18	0.0358	0.3285	-0.5720	0.0	0.58	0.1028	0.0388	-0.1680	60.8
1	0.94	0.1714	0.033	-0.0669	94.6	0.21	0.0368	0.6196	-0.7863	0.0	0.71	0.1199	0.0988	-0.2905	27.6

Table S2: Association parameters for varying measurement error with 50% censoring

True association	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.25															
0	0.00	0.0713	0.0051	-0.0025	94.2	0.00	0.0605	0.0037	-0.0018	95.0	0.00	0.0713	0.0051	-0.0025	94.2
0.25	0.25	0.0677	0.0046	-0.0017	94.6	0.20	0.0551	0.0059	-0.0531	84.2	0.25	0.0668	0.0045	-0.0027	94.8
0.50	0.50	0.0736	0.0054	-0.0037	94.8	0.39	0.0575	0.0161	-0.1131	50.2	0.49	0.0699	0.0050	-0.0124	94.6
0.75	0.74	0.0840	0.0071	-0.0086	95.4	0.56	0.0624	0.0387	-0.1866	16.4	0.71	0.0755	0.0070	-0.0364	90.2
1	0.98	0.0989	0.0100	-0.0162	95.2	0.72	0.0705	0.0810	-0.2757	3.2	0.92	0.0835	0.0129	-0.0769	83.6
Measurement error $\sigma_e^2 =$ 0.5															
0	0.00	0.0738	0.0054	-0.0027	94.6	0.00	0.0550	0.0030	-0.0015	94.6	0.00	0.0732	0.0054	-0.0026	94.6
0.25	0.25	0.0718	0.0052	-0.0023	94.8	0.16	0.0499	0.0101	-0.0872	56.2	0.24	0.0696	0.0049	-0.0060	94.6
0.50	0.49	0.0806	0.0065	-0.0059	95.2	0.32	0.0521	0.0367	-0.1844	6.4	0.48	0.0733	0.0060	-0.0241	93.6
0.75	0.74	0.0952	0.0093	-0.0138	93.4	0.45	0.0564	0.0921	-0.2982	0.0	0.69	0.0795	0.0104	-0.0641	85.4
1	0.97	0.1136	0.0136	-0.0264	94.6	0.57	0.0631	0.1884	-0.4295	0.0	0.87	0.0871	0.0239	-0.1277	67.6
Measurement error $\sigma_e^2 =$ 1.0															
0	0.00	0.0773	0.0060	-0.0028	94.4	0.00	0.0472	0.0022	-0.0011	95.0	0.00	0.0754	0.0057	-0.0027	94.4
0.25	0.25	0.0788	0.0062	-0.0034	95.4	0.12	0.0431	0.0185	-0.1292	15.8	0.24	0.0737	0.0056	-0.0126	93.4
0.50	0.49	0.0920	0.0085	-0.0089	95.2	0.23	0.0449	0.0745	-0.2693	0.0	0.46	0.0788	0.0081	-0.0435	90.8
0.75	0.73	0.1137	0.0133	-0.0200	95.2	0.32	0.0480	0.1837	-0.4260	0.0	0.65	0.0866	0.0182	-0.1035	77.8
1	0.96	0.1400	0.0211	-0.0386	95.4	0.40	0.0530	0.3601	-0.5977	0.0	0.81	0.0938	0.0462	-0.1933	43.6
Measurement error $\sigma_e^2 =$ 1.5															
0	0.00	0.0802	0.0064	-0.0028	94.2	0.00	0.0420	0.0018	-0.0008	94.8	0.00	0.0768	0.0059	-0.0027	94.6
0.25	0.25	0.0847	0.0072	-0.0041	94.4	0.10	0.0386	0.0252	-0.1540	2.0	0.23	0.0768	0.0062	-0.0184	93.0
0.50	0.49	0.1014	0.0104	-0.0110	95.2	0.18	0.0401	0.1029	-0.3183	0.0	0.44	0.0832	0.0104	-0.0587	88.8
0.75	0.73	0.1289	0.0172	-0.0236	94.4	0.25	0.0425	0.2491	-0.4973	0.0	0.62	0.0929	0.0259	-0.1314	69.6
1	0.95	0.1594	0.0278	-0.0486	94.0	0.31	0.0463	0.4759	-0.6883	0.0	0.76	0.1002	0.0660	-0.2366	32.8
Measurement error $\sigma_e^2 =$ 2.0															
0	0.00	0.0827	0.0068	-0.0028	95.0	0.00	0.0381	0.0015	-0.0007	94.8	0.00	0.0779	0.0061	-0.0026	94.4
0.25	0.25	0.0895	0.0080	-0.0047	94.4	0.08	0.0353	0.0303	-0.1703	0.2	0.23	0.0794	0.0068	-0.0233	92.4
0.50	0.49	0.1088	0.0120	-0.0136	95.2	0.15	0.0365	0.1239	-0.3501	0.0	0.43	0.0870	0.0126	-0.0711	86.4
0.75	0.73	0.1485	0.0225	-0.0209	95.4	0.21	0.0380	0.2914	-0.5385	0.0	0.60	0.1042	0.0323	-0.1464	70.2

True association	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\mathrm{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
1	0.96	0.1876	0.0371	-0.0433	94.0	0.26	0.0397	0.5533	-0.7428	0.0	0.74	0.1156	0.0799	-0.2579	33.0
Measurement error $\sigma_e^2 =$ 2.5															
0	0.00	0.0850	0.0072	-0.0028	94.6	0.00	0.0352	0.0012	-0.0006	94.2	0.00	0.0791	0.0063	-0.0025	94.8
0.25	0.24	0.0935	0.0088	-0.0052	94.6	0.07	0.0328	0.0342	-0.1820	0.0	0.22	0.0816	0.0074	-0.0274	92.6
0.50	0.48	0.1153	0.0136	-0.0161	94.8	0.13	0.0338	0.1399	-0.3724	0.0	0.42	0.0907	0.0149	-0.0813	84.4
0.75	0.72	0.1484	0.0229	-0.0300	94.8	0.18	0.0358	0.3285	-0.5720	0.0	0.58	0.1028	0.0388	-0.1680	60.8
1	0.93	0.1882	0.0399	-0.0669	94.6	0.21	0.0368	0.6196	-0.7863	0.0	0.71	0.1199	0.0988	-0.2905	27.6

Table S3: Association parameters for varying measurement error with 70% censoring

True association	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\mathrm{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.25															
0	0.00	0.0850	0.0072	-0.0040	95.2	0.00	0.0714	0.0051	-0.0028	94.4	0.00	0.0852	0.0073	-0.0040	95.2
0.25	0.25	0.0986	0.0097	-0.0023	94.4	0.20	0.0814	0.0090	-0.0486	91.4	0.25	0.0977	0.0095	-0.0028	95.0
0.50	0.49	0.1027	0.0106	-0.0056	95.6	0.39	0.0808	0.0182	-0.1080	72.6	0.49	0.0990	0.0099	-0.0116	95.4
0.75	0.74	0.1119	0.0126	-0.0092	94.4	0.58	0.0846	0.0376	-0.1746	41.8	0.72	0.1035	0.0116	-0.0299	93.8
1	0.98	0.1195	0.0145	-0.0163	94.2	0.75	0.0844	0.0701	-0.2509	16.6	0.94	0.1051	0.0149	-0.0618	90.6
Measurement error $\sigma_e^2 =$ 0.5															
0	0.00	0.0893	0.0080	-0.0036	95.2	0.00	0.0657	0.0043	-0.0019	94.8	0.00	0.0884	0.0078	-0.0036	95.4
0.25	0.25	0.1047	0.0110	-0.0042	94.4	0.17	0.0739	0.0124	-0.0831	80.8	0.24	0.1016	0.0104	-0.0082	94.0
0.50	0.49	0.1129	0.0128	-0.0086	95.8	0.32	0.0739	0.0369	-0.1774	32.8	0.48	0.1044	0.0115	-0.0247	94.0
0.75	0.73	0.1255	0.0160	-0.0151	94.8	0.47	0.0768	0.0868	-0.2845	4.6	0.69	0.1084	0.0152	-0.0587	92.0
1	0.97	0.1384	0.0199	-0.0270	94.0	0.60	0.0754	0.1667	-0.4013	0.2	0.89	0.1103	0.0246	-0.1114	82.8
Measurement error $\sigma_e^2 =$ 1.0															
0	0.01	0.1047	0.0110	0.0061	92.8	0.00	0.0612	0.0037	0.0012	94.0	0.01	0.1008	0.0102	0.0057	93.0
0.25	0.24	0.1138	0.0130	-0.0070	94.4	0.12	0.0636	0.0198	-0.1256	48.8	0.23	0.1065	0.0117	-0.0178	93.4
0.50	0.49	0.1276	0.0165	-0.0143	95.2	0.24	0.0637	0.0725	-0.2616	2.2	0.45	0.1105	0.0145	-0.0477	92.4
0.75	0.72	0.1428	0.0210	-0.0253	95.2	0.34	0.0625	0.1725	-0.4106	0.0	0.65	0.1130	0.0228	-0.0999	86.6
1	0.96	0.1685	0.0303	-0.0437	94.0	0.43	0.0638	0.3306	-0.5714	0.0	0.82	0.1196	0.0467	-0.1800	67.4
Measurement error $\sigma_e^2 =$ 1.5															

True association	Proposed joint model					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
	$\hat{\gamma}_t$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov	$\hat{\alpha}$	SE	MSE	Bias	Cov
0	0.01	0.1108	0.0123	0.0066	93.2	0.00	0.0549	0.0030	0.0009	94.4	0.01	0.1043	0.0109	0.0060	94.2
0.25	0.24	0.1212	0.0148	-0.0090	95.0	0.10	0.0566	0.0260	-0.1508	24.6	0.22	0.1100	0.0128	-0.0254	93.2
0.50	0.48	0.1428	0.0208	-0.0193	95.2	0.19	0.0598	0.1018	-0.3134	0.0	0.43	0.1188	0.0185	-0.0664	91.8
0.75	0.71	0.1669	0.0741	-0.0351	94.6	0.26	0.0547	0.2401	-0.4869	0.0	0.61	0.1259	0.0341	-0.1352	79.8
1	0.93	0.2011	0.0451	-0.0684	88.6	0.33	0.0595	0.4513	-0.6691	0.0	0.77	0.1259	0.0711	-0.2350	51.2
Measurement error $\sigma_e^2 = 2.0$															
0	0.00	0.1148	0.0132	0.0018	95.6	0.00	0.0489	0.0024	0.0004	95.4	0.00	0.1067	0.0114	0.0016	96.4
0.25	0.24	0.1231	0.0153	-0.0120	94.8	0.08	0.0500	0.0311	-0.1690	8.4	0.22	0.1096	0.0131	-0.0324	94.2
0.50	0.48	0.1434	0.0210	-0.0213	94.2	0.16	0.0493	0.1203	-0.3433	0.0	0.42	0.1148	0.0193	-0.0781	90.8
0.75	0.71	0.1808	0.0341	-0.0378	95.0	0.22	0.0505	0.2837	-0.5302	0.0	0.60	0.1296	0.0398	-0.1517	77.4
1	0.93	0.2231	0.0551	-0.0730	95.6	0.27	0.0535	0.5357	-0.7299	0.0	0.74	0.1429	0.0882	-0.2603	50.4
Measurement error $\sigma_e^2 = 2.5$															
0	0.00	0.1197	0.0143	-0.0047	95.6	0.00	0.0468	0.0022	-0.0021	94.0	0.00	0.1086	0.0118	-0.0046	96.4
0.25	0.24	0.1235	0.0154	-0.0140	95.2	0.07	0.0450	0.0343	-0.1797	1.6	0.21	0.1059	0.0126	-0.0371	94.2
0.50	0.47	0.1531	0.0242	-0.0274	94.6	0.13	0.0473	0.1381	-0.3686	0.0	0.41	0.1236	0.0235	-0.0906	90.0
0.75	0.70	0.1945	0.0401	-0.0480	95.4	0.18	0.0489	0.3219	-0.5653	0.0	0.58	0.1416	0.0497	-0.1722	77.2
1	0.92	0.2332	0.0614	-0.0838	93.2	0.23	0.0462	0.5928	-0.7685	0.0	0.71	0.1465	0.1059	-0.2906	46.4

Table S4: C-Index for varying measurement error with 30% censoring

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 = 0.25$																
0	0.5117 (0.0089)	0.51	0.0090	0.000	0.000	95.4	0.51	0.0091	0.000	0.000	96.0	0.51	0.0570	0.000	0.000	95.6
0.25	0.5698 (0.0148)	0.56	0.0152	0.000	-0.005	94.0	0.56	0.0152	0.000	-0.008	92.4	0.56	0.0150	0.000	-0.005	93.8
0.50	0.6353 (0.0151)	0.63	0.0162	0.000	-0.010	91.8	0.62	0.0157	0.001	-0.017	80.4	0.62	0.0155	0.000	-0.012	88.6
0.75	0.6928 (0.0148)	0.68	0.0165	0.001	-0.014	85.6	0.67	0.0156	0.001	-0.028	56.6	0.67	0.0155	0.001	-0.019	73.8
1	0.7415 (0.0147)	0.72	0.0167	0.001	-0.019	80.8	0.70	0.0157	0.002	-0.039	32.4	0.71	0.0155	0.001	-0.028	53.4
Measurement error $\sigma_e^2 = 0.5$																
0	0.5117 (0.0089)	0.51	0.0090	0.000	0.000	95.2	0.51	0.0092	0.000	0.000	95.6	0.51	0.0090	0.000	-0.001	95.4
0.25	0.5697 (0.0148)	0.56	0.0155	0.000	-0.008	92.6	0.56	0.0153	0.000	-0.013	85.0	0.56	0.0150	0.000	-0.009	92.0
0.50	0.6353 (0.0151)	0.62	0.0169	0.001	-0.015	85.8	0.61	0.0157	0.001	-0.029	54.4	0.62	0.0155	0.001	-0.019	74.2
0.75	0.6929 (0.0151)	0.67	0.0176	0.001	-0.022	74.8	0.65	0.0159	0.002	-0.046	17.4	0.66	0.0157	0.001	-0.032	47.0
1	0.7415 (0.0147)	0.71	0.0180	0.001	-0.028	64.4	0.68	0.0161	0.004	-0.063	2.2	0.70	0.0157	0.002	-0.045	17.0
Measurement error $\sigma_e^2 = 1.0$																
0	0.5117 (0.0089)	0.51	0.0093	0.000	-0.000	95.0	0.51	0.0094	0.000	0.000	95.8	0.51	0.0090	0.000	-0.000	94.6
0.25	0.5697 (0.0148)	0.56	0.0158	0.000	-0.011	89.2	0.55	0.0153	0.001	-0.021	72.4	0.56	0.0147	0.000	-0.014	84.2
0.50	0.6352 (0.0151)	0.61	0.0176	0.001	-0.022	76.2	0.59	0.0155	0.002	-0.045	16.2	0.61	0.0152	0.001	-0.030	49.2
0.75	0.6929 (0.0151)	0.66	0.0189	0.001	-0.031	61.6	0.62	0.0158	0.005	-0.069	1.2	0.64	0.0157	0.003	-0.048	13.4
1	0.7415 (0.0147)	0.70	0.0200	0.002	-0.039	48.4	0.65	0.0162	0.009	-0.094	0.0	0.65	0.0157	0.005	-0.068	1.0
Measurement error $\sigma_e^2 = 1.5$																
0	0.5117 (0.0089)	0.51	0.0093	0.000	-0.000	94.6	0.51	0.0094	0.000	0.000	95.8	0.51	0.0089	0.000	-0.001	95.0
0.25	0.5695 (0.0149)	0.56	0.0152	0.000	-0.014	83.8	0.54	0.0144	0.001	-0.027	53.0	0.55	0.0138	0.001	-0.017	77.6
0.50	0.6353 (0.0151)	0.61	0.0183	0.001	-0.026	69.2	0.58	0.0156	0.003	-0.055	6.4	0.60	0.0151	0.002	-0.037	30.4
0.75	0.6929 (0.0151)	0.66	0.0200	0.002	-0.037	53.0	0.61	0.0158	0.007	-0.084	0.0	0.63	0.0157	0.004	-0.060	2.8
1	0.7415 (0.0147)	0.70	0.0221	0.003	-0.046	42.8	0.63	0.0162	0.013	-0.112	0.0	0.66	0.0157	0.007	-0.084	0.0
Measurement error $\sigma_e^2 = 2.0$																
0	0.5117 (0.0089)	0.51	0.0094	0.000	-0.000	95.4	0.51	0.0095	0.000	0.000	96.2	0.51	0.0089	0.000	-0.001	95.6
0.25	0.5695 (0.0149)	0.55	0.0154	0.001	-0.016	81.8	0.54	0.0145	0.001	-0.031	42.2	0.55	0.0136	0.001	-0.020	68.6
0.50	0.6353 (0.0151)	0.61	0.0188	0.001	-0.030	65.0	0.57	0.0155	0.004	-0.062	2.4	0.59	0.0150	0.002	-0.043	19.2
0.75	0.6929 (0.0151)	0.65	0.0280	0.003	-0.042	45.6	0.60	0.0157	0.009	-0.095	0.0	0.62	0.0158	0.005	-0.069	0.4
1	0.7415 (0.0146)	0.69	0.0235	0.003	-0.052	35.8	0.62	0.0161	0.016	-0.125	0.0	0.65	0.0157	0.009	-0.095	0.0
Measurement error $\sigma_e^2 = 2.5$																
0	0.5117 (0.0089)	0.51	0.0093	0.000	-0.000	95.4	0.51	0.0095	0.000	0.000	96.6	0.51	0.0087	0.000	-0.001	95.4
0.25	0.5697 (0.0158)	0.55	0.0169	0.001	-0.018	81.2	0.54	0.0152	0.001	-0.033	41.2	0.55	0.0146	0.001	-0.023	65.8
0.50	0.6353 (0.0151)	0.60	0.0193	0.001	-0.033	59.6	0.57	0.0154	0.005	-0.068	1.2	0.59	0.0148	0.003	-0.048	11.0

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
0.75	0.6929 (0.0151)	0.65	0.0219	0.003	-0.046	41.0	0.59	0.0156	0.011	-0.103	0.0	0.62	0.0158	0.006	-0.076	0.0
1	0.7415 (0.0147)	0.68	0.0249	0.004	-0.057	33.4	0.61	0.0161	0.018	-0.135	0.0	0.64	0.0160	0.011	-0.104	0.0

Table S5: C-Index for varying measurement error with 50% censoring

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.25																
0	0.5149 (0.0115)	0.51	0.0114	0.0001	-0.0003	94.8	0.52	0.0116	0.0001	0.0001	95.8	0.51	0.0114	0.0001	-0.0003	94.8
0.25	0.5694 (0.0176)	0.56	0.0172	0.0003	-0.0053	93.6	0.56	0.0170	0.0004	-0.0080	91.4	0.56	0.0170	0.0003	-0.0055	93.2
0.50	0.6352 (0.0173)	0.62	0.0176	0.0004	-0.0105	91.2	0.62	0.0170	0.0006	-0.0171	82.2	0.62	0.0170	0.0004	-0.0121	88.4
0.75	0.6930 (0.0169)	0.68	0.0179	0.0006	-0.0154	85.6	0.67	0.0172	0.0010	-0.0271	62.6	0.67	0.0170	0.0007	-0.0198	78.8
1	0.7412 (0.0169)	0.72	0.0187	0.0007	-0.0197	81.6	0.70	0.0183	0.0017	-0.0368	48.4	0.71	0.0176	0.0011	-0.0276	65.8
Measurement error $\sigma_e^2 =$ 0.5																
0	0.5149 (0.0115)	0.51	0.0114	0.0001	-0.0006	95.2	0.52	0.0115	0.0001	0.0001	95.0	0.51	0.0113	0.0001	-0.0007	95.2
0.25	0.5694 (0.0176)	0.56	0.0174	0.0004	-0.0082	920	0.56	0.0169	0.0005	-0.0137	87.2	0.56	0.0169	0.0004	-0.0091	90.8
0.50	0.6352 (0.0173)	0.62	0.0182	0.0006	-0.0161	85.0	0.61	0.0170	0.0011	-0.0291	59.0	0.62	0.0170	0.0007	-0.0200	78.0
0.75	0.6930 (0.0169)	0.67	0.0190	0.0009	-0.0233	77.2	0.65	0.0174	0.0023	-0.0452	28.0	0.66	0.0172	0.0013	-0.0325	52.8
1	0.7412 (0.0169)	0.71	0.0200	0.0013	-0.0294	68.4	0.68	0.0188	0.0040	-0.0603	10.8	0.70	0.0177	0.0023	-0.0450	28.0
Measurement error $\sigma_e^2 =$ 1.0																
0	0.5149 (0.0115)	0.51	0.0113	0.0001	-0.0009	96.0	0.51	0.0114	0.0001	0.0000	95.4	0.51	0.0109	0.0001	-0.0012	96.0
0.25	0.5694 (0.0176)	0.56	0.0178	0.0005	-0.0120	89.6	0.55	0.0169	0.0008	-0.0215	75.6	0.56	0.0167	0.0005	-0.0142	86.2
0.50	0.6352 (0.0173)	0.61	0.0192	0.0009	-0.0232	76.8	0.59	0.0171	0.0023	-0.0450	26.8	0.60	0.0169	0.0012	-0.0309	55.0
0.75	0.6930 (0.0169)	0.66	0.0207	0.0015	-0.0332	63.0	0.62	0.0176	0.0050	-0.0686	3.4	0.64	0.0172	0.0028	-0.0496	19.0
1	0.7412 (0.0169)	0.70	0.0223	0.0022	-0.0413	53.4	0.65	0.0191	0.0084	-0.0898	0.4	0.67	0.0178	0.0050	-0.0682	3.6
Measurement error $\sigma_e^2 =$ 1.5																
0	0.5149 (0.0115)	0.51	0.0112	0.0001	-0.0010	96.2	0.51	0.0113	0.0001	-0.0001	95.4	0.51	0.0106	0.0001	-0.0015	96.4
0.25	0.5694 (0.0176)	0.55	0.0181	0.0005	-0.0145	87.6	0.54	0.0170	0.0010	-0.0268	64.8	0.55	0.0165	0.0006	-0.0179	81.0
0.50	0.6352 (0.0173)	0.61	0.0199	0.0012	-0.0281	70.4	0.58	0.0172	0.0034	-0.0554	10.6	0.60	0.0167	0.0018	-0.0386	38.0
0.75	0.6930 (0.0169)	0.65	0.0221	0.0021	-0.0398	55.4	0.61	0.0177	0.0073	-0.0836	0.4	0.63	0.0172	0.0041	-0.0615	3.8
1	0.7412 (0.0169)	0.69	0.0240	0.0030	-0.0494	44.0	0.63	0.0191	0.0121	-0.1082	0.0	0.66	0.0177	0.0074	-0.0841	0.4
Measurement error $\sigma_e^2 =$ 2.0																
0	0.5149 (0.0115)	0.51	0.0112	0.0001	-0.0011	96.2	0.51	0.0113	0.0001	-0.0002	95.2	0.51	0.0104	0.0001	-0.0018	97.0
0.25	0.5694 (0.0176)	0.55	0.0183	0.0006	-0.0165	85.2	0.54	0.0170	0.0012	-0.0307	54.2	0.55	0.0163	0.0007	-0.0208	75.6
0.50	0.6352 (0.0173)	0.60	0.0204	0.0014	-0.0320	64.0	0.57	0.0173	0.0043	-0.0629	5.6	0.59	0.0166	0.0023	-0.0447	24.6
0.75	0.6938 (0.0164)	0.65	0.0231	0.0026	-0.0452	49.4	0.60	0.0176	0.0090	-0.0930	0.0	0.62	0.0174	0.0053	-0.0706	2.4
1	0.7412 (0.0156)	0.69	0.0253	0.0036	-0.0548	40.0	0.62	0.0179	0.0148	-0.1203	0.0	0.65	0.0181	0.0094	-0.0951	0.0

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 2.5																
0	0.5149 (0.0115)	0.51	0.0112	0.0001	-0.0012	96.4	0.51	0.0114	0.0001	-0.0003	95.4	0.51	0.0102	0.0001	-0.0020	96.8
0.25	0.5694 (0.0176)	0.55	0.0184	0.0007	-0.0182	83.6	0.54	0.0169	0.0014	-0.0336	46.0	0.55	0.0161	0.0008	-0.0231	72.2
0.50	0.6352 (0.0173)	0.60	0.0209	0.0017	-0.0353	2.8	0.57	0.0173	0.0050	-0.0686	0.2	0.59	0.0165	0.0027	-0.0496	0.0
0.75	0.6937 (0.0167)	0.64	0.0244	0.0030	-0.0490	46.6	0.59	0.0182	0.0107	-0.1019	0.0	0.62	0.0181	0.0063	-0.0774	1.0
1	0.7412 (0.0158)	0.68	0.0266	0.0045	-0.0614	34.8	0.61	0.0180	0.0178	-0.1320	0.0	0.64	0.0175	0.0114	-0.1055	0.0

Table S6: C-Index for varying measurement error with 70% censoring

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
Measurement error $\sigma_e^2 =$ 0.25																
0	0.5180 (0.0138)	0.52	0.0136	0.0002	-0.0007	96.0	0.52	0.0138	0.0002	-0.0004	95.4	0.52	0.0136	0.0002	-0.0006	96.0
0.25	0.5075 (0.0245)	0.56	0.0246	0.0006	-0.0065	93.0	0.56	0.0245	0.0007	-0.0077	93.0	0.56	0.0245	0.0006	-0.0066	93.2
0.50	0.6351 (0.0229)	0.62	0.0240	0.0007	-0.0112	92.0	0.62	0.0236	0.0008	-0.0157	89.6	0.62	0.0235	0.0007	-0.0122	91.0
0.75	0.6937 (0.0221)	0.68	0.0234	0.0008	-0.0169	89.2	0.67	0.0229	0.0011	-0.0247	83.2	0.67	0.0227	0.0009	-0.0197	87.0
1	0.7419 (0.0190)	0.72	0.0206	0.0009	-0.0213	82.6	0.71	0.0201	0.0014	-0.0320	65.4	0.72	0.0199	0.0011	-0.0262	74.6
Measurement error $\sigma_e^2 =$ 0.5																
0	0.5180 (0.0138)	0.52	0.0136	0.0002	-0.0007	95.6	0.52	0.0138	0.0002	-0.0002	94.8	0.52	0.0134	0.0002	-0.0008	95.8
0.25	0.5075 (0.0245)	0.56	0.0248	0.0007	-0.0096	91.8	0.56	0.0243	0.0008	-0.0132	91.0	0.56	0.0242	0.0007	-0.0106	91.8
0.50	0.6351 (0.0229)	0.62	0.0248	0.0009	-0.0171	89.0	0.61	0.0239	0.0013	-0.0269	78.4	0.61	0.0235	0.0010	-0.0204	85.4
0.75	0.6937 (0.0221)	0.67	0.0247	0.0013	-0.0253	83.4	0.65	0.0234	0.0023	-0.0418	56.4	0.66	0.0228	0.0016	-0.0329	74.0
1	0.7419 (0.0190)	0.71	0.0222	0.0015	-0.0316	72.6	0.69	0.0209	0.0033	-0.0537	27.4	0.70	0.0202	0.0023	-0.0436	44.2
Measurement error $\sigma_e^2 =$ 1.0																
0	0.5186 (0.0145)	0.52	0.0155	0.0002	0.0001	94.6	0.52	0.0154	0.0002	0.0001	95.0	0.52	0.0148	0.0002	-0.0005	95.2
0.25	0.5075 (0.0245)	0.56	0.0251	0.0008	-0.0137	90.6	0.55	0.0236	0.0010	-0.0206	86.0	0.55	0.0237	0.0008	-0.0163	89.0
0.50	0.6351 (0.0229)	0.61	0.0259	0.0013	-0.0251	84.0	0.59	0.0241	0.0024	-0.0421	59.4	0.60	0.0233	0.0016	-0.0323	96.0
0.75	0.6934	0.66	0.0251	0.0019	-0.0360	70.6	0.63	0.0229	0.0046	-0.0635	22.6	0.64	0.0218	0.0030	-0.0502	34.8
1	0.7419 (0.0190)	0.70	0.0248	0.0026	-0.0450	56.8	0.66	0.0217	0.0072	-0.0821	3.8	0.67	0.0205	0.0050	-0.0679	8.2
Measurement error $\sigma_e^2 =$ 1.5																
0	0.5186 (0.0145)	0.52	0.0157	0.0002	0.0002	94.0	0.52	0.0153	0.0002	0.0003	95.0	0.52	0.0146	0.0002	-0.0008	95.4
0.25	0.5075 (0.0245)	0.55	0.0254	0.0009	-0.0165	89.6	0.55	0.0228	0.0012	-0.0254	78.0	0.55	0.0233	0.0010	-0.0202	86.0
0.50	0.6364 (0.0253)	0.60	0.0284	0.0018	-0.0320	81.0	0.58	0.0260	0.0036	-0.0541	45.4	0.59	0.0245	0.0024	-0.0421	60.4
0.75	0.6922 (0.0210)	0.65	0.0271	0.0026	-0.0433	64.8	0.61	0.0224	0.0067	-0.0786	6.8	0.63	0.0223	0.0044	-0.0627	20.8
1	0.7424 (0.0194)	0.69	0.0279	0.0039	-0.0558	44.4	0.64	0.0232	0.0111	-0.1026	1.0	0.66	0.0214	0.0078	-0.0855	3.0
Measurement error $\sigma_e^2 =$ 2.0																
0	0.5199 (0.0157)	0.52	0.0150	0.0002	-0.0005	95.6	0.52	0.0146	0.0002	-0.0012	95.5	0.52	0.0138	0.0002	-0.0018	96.4

True γ	True C-Index (SE)	Proposed measurement error adjusted estimator $\hat{M}$					Observed biomarker y_0					LME estimator $(\hat{U}_0)_{\text{lme}}$				
		C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov	C-Index	SE	MSE	Bias	Cov
0.25	0.5693 (0.0245)	0.55	0.0242	0.0010	-0.0194	86.4	0.54	0.0223	0.0014	-0.0300	72.2	0.55	0.0216	0.0010	-0.0238	78.8
0.50	0.6347 (0.0218)	0.60	0.0253	0.0019	-0.0350	68.2	0.58	0.0233	0.0041	-0.0592	24.8	0.59	0.0211	0.0026	-0.0468	35.2
0.75	0.6935 (0.0207)	0.64	0.0280	0.0033	-0.0500	55.4	0.60	0.0234	0.0085	-0.0890	3.4	0.62	0.0218	0.0057	-0.0722	9.6
1	0.7419 (0.0205)	0.68	0.0310	0.0048	-0.0620	47.4	0.63	0.0241	0.0138	-0.1149	0.0	0.64	0.0230	0.0100	-0.0971	1.2
Measurement error $\sigma_e^2 = 2.5$																
0	0.5194 (0.0146)	0.52	0.0148	0.0002	-0.0006	96.8	0.52	0.0143	0.0002	0.0000	94.2	0.52	0.0134	0.0002	-0.0021	97.4
0.25	0.5686 (0.0225)	0.55	0.0233	0.0010	-0.0217	87.0	0.54	0.0216	0.0015	-0.0325	66.6	0.54	0.0203	0.0011	-0.0265	75.8
0.50	0.6354 (0.0234)	0.60	0.0270	0.0023	-0.0399	69.4	0.57	0.0241	0.0050	-0.0668	20.4	0.58	0.0220	0.0033	-0.0531	32.0
0.75	0.6937 (0.0221)	0.64	0.0296	0.0040	-0.0562	52.8	0.60	0.0244	0.0103	-0.0984	1.8	0.61	0.0225	0.0071	-0.0809	5.2
1	0.7409 (0.0203)	0.67	0.0316	0.0055	-0.0674	40.2	0.62	0.0219	0.0157	-0.1233	0.0	0.63	0.0224	0.0119	-0.1066	0.4

Table S7: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0 and 30% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.5114 (0.0089)	0.5111 (0.0086)	0.0001	-0.0003	95.2	0.5079 (0.0061)	0.5079 (0.0062)	0.5112 (0.0083)	0.0001	-0.0002	94.2	0.5079 (0.0060)	0.5079 (0.0059)
2	0.5114 (0.0089)	0.5111 (0.0086)	0.0001	-0.0003	95.4	0.5079 (0.0063)	0.5079 (0.0061)	0.5112 (0.0083)	0.0001	-0.0002	94.2	0.5078 (0.0061)	0.5080 (0.0059)
3	0.5113 (0.0088)	0.5111 (0.0085)	0.0001	-0.0003	95.0	0.5078 (0.0067)	0.5079 (0.0063)	0.5111 (0.0082)	0.0001	-0.0002	94.0	0.5079 (0.0065)	0.5078 (0.0061)
4	0.5107 (0.0082)	0.5106 (0.0082)	0.0001	0.0000	94.8	0.5022 (0.0175)	0.5130 (0.0139)	0.5105 (0.0078)	0.0001	-0.0001	95.2	0.5020 (0.0173)	0.5131 (0.0141)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.5114 (0.0089)	0.5111 (0.0087)	0.0001	-0.0003	95.0	0.5079 (0.0062)	0.5078 (0.0062)	0.5112 (0.0082)	0.0001	-0.0002	95.0	0.5079 (0.0059)	0.5080 (0.0059)
2	0.5114 (0.0089)	0.5111 (0.0087)	0.0001	-0.0003	95.2	0.5079 (0.0063)	0.5078 (0.0062)	0.5112 (0.0082)	0.0001	-0.0002	94.8	0.5079 (0.0060)	0.5079 (0.0059)
3	0.5113 (0.0088)	0.5111 (0.0086)	0.0001	-0.0003	95.4	0.5078 (0.0067)	0.5078 (0.0064)	0.5111 (0.0082)	0.0001	-0.0002	95.0	0.5080 (0.0064)	0.5078 (0.0060)
4	0.5107 (0.0082)	0.5106 (0.0083)	0.0001	0.0000	95.2	0.5020 (0.0175)	0.5132 (0.0140)	0.5106 (0.0079)	0.0001	-0.0001	95.2	0.5020 (0.0175)	0.5132 (0.0142)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.5114 (0.0089)	0.5112 (0.0088)	0.0001	-0.0003	94.8	0.5079 (0.0064)	0.5079 (0.0062)	0.5113 (0.0083)	0.0001	-0.0001	95.0	0.5080 (0.0059)	0.5080 (0.0059)
2	0.5114 (0.0089)	0.5112 (0.0088)	0.0001	-0.0002	95.2	0.5079 (0.0064)	0.5080 (0.0063)	0.5113 (0.0082)	0.0001	-0.0001	95.0	0.5079 (0.0060)	0.5081 (0.0059)
3	0.5113 (0.0088)	0.5111 (0.0088)	0.0001	-0.0002	95.0	0.5078 (0.0070)	0.5080 (0.0065)	0.5113 (0.0082)	0.0001	-0.0001	95.2	0.5079 (0.0063)	0.5081 (0.0063)
4	0.5107 (0.0082)	0.5108 (0.0084)	0.0001	0.0000	95.4	0.5020 (0.0177)	0.5133 (0.0141)	0.5107 (0.0080)	0.0001	0.0000	95.4	0.5021 (0.0178)	0.5132 (0.0141)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.5114 (0.0089)	0.5112 (0.0088)	0.0001	-0.0002	95.2	0.5080 (0.0064)	0.5079 (0.0062)	0.5114 (0.0083)	0.0001	0.0000	95.0	0.5081 (0.0060)	0.5082 (0.0059)
2	0.5114 (0.0089)	0.5114 (0.0089)	0.0001	0.0000	95.4	0.5080 (0.0064)	0.5081 (0.0064)	0.5114 (0.0083)	0.0001	0.0000	95.0	0.5080 (0.0060)	0.5082 (0.0060)
3	0.5113 (0.0088)	0.5113 (0.0088)	0.0001	0.0000	95.2	0.5080 (0.0070)	0.5080 (0.0064)	0.5114 (0.0082)	0.0001	0.0000	94.8	0.5079 (0.0063)	0.5082 (0.0063)
4	0.5107 (0.0082)	0.5108 (0.0085)	0.0001	0.0001	95.0	0.5022 (0.0178)	0.5133 (0.0141)	0.5108 (0.0080)	0.0001	0.0001	95.8	0.5022 (0.0179)	0.5133 (0.0142)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5114 (0.0089)	0.5113 (0.0088)	0.0001	-0.0001	95.4	0.5080 (0.0063)	0.5080 (0.0063)	0.5115 (0.0083)	0.0001	0.0001	95.2	0.5081 (0.0060)	0.5082 (0.0059)
2	0.5114 (0.0089)	0.5115 (0.0089)	0.0001	0.0001	95.4	0.5081 (0.0065)	0.5082 (0.0063)	0.5115 (0.0083)	0.0001	0.0001	95.2	0.5081 (0.0061)	0.5082 (0.0060)
3	0.5113 (0.0088)	0.5115 (0.0089)	0.0001	0.0001	95.2	0.5082 (0.0071)	0.5081 (0.0064)	0.5115 (0.0083)	0.0001	0.0001	94.8	0.5081 (0.0064)	0.5081 (0.0063)
4	0.5107 (0.0082)	0.5109 (0.0085)	0.0001	0.0002	94.6	0.5024 (0.0179)	0.5132 (0.0141)	0.5109 (0.0081)	0.0001	0.0002	96.2	0.5023 (0.0179)	0.5133 (0.0142)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.5121 (0.0089)	0.5115 (0.0089)	0.0001	-0.0006	95.6	0.5081 (0.0064)	0.5081 (0.0063)	0.5117 (0.0086)	0.0001	-0.0004	96.4	0.5082 (0.0061)	0.5084 (0.0062)
2	0.5120 (0.0088)	0.5117 (0.0091)	0.0001	-0.0003	94.8	0.5082 (0.0066)	0.5083 (0.0065)	0.5117 (0.0086)	0.0001	-0.0004	96.2	0.5083 (0.0062)	0.5082 (0.0062)
3	0.5120 (0.0088)	0.5118 (0.0091)	0.0001	-0.0003	95.4	0.5082 (0.0071)	0.5085 (0.0068)	0.5117 (0.0086)	0.0001	-0.0004	96.0	0.5082 (0.0066)	0.5083 (0.0064)
4	0.5115 (0.0088)	0.5112 (0.0089)	0.0001	-0.0003	95.0	0.5030 (0.0179)	0.5130 (0.0145)	0.5110 (0.0084)	0.0001	-0.0005	95.8	0.5033 (0.0174)	0.5125 (0.0142)

Table S8: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0.25 and 30% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.5701 (0.0146)	0.5652 (0.0144)	0.0002	-0.0049	93.0	0.5464 (0.0105)	0.5460 (0.0104)	0.5630 (0.0141)	0.0003	-0.0071	91.4	0.5447 (0.0102)	0.5446 (0.0102)
2	0.5694 (0.0143)	0.5646 (0.0141)	0.0002	-0.0048	93.4	0.5461 (0.0105)	0.5456 (0.0103)	0.5625 (0.0138)	0.0002	-0.0070	91.6	0.5444 (0.0101)	0.5442 (0.0101)
3	0.5677 (0.0139)	0.5630 (0.0137)	0.0002	-0.0047	92.8	0.5450 (0.0106)	0.5446 (0.0104)	0.5611 (0.0135)	0.0002	-0.0066	91.2	0.5436 (0.0106)	0.5433 (0.0101)
4	0.5626 (0.0154)	0.5581 (0.0147)	0.0002	-0.0045	94.4	0.5425 (0.0189)	0.5410 (0.0183)	0.5568 (0.0150)	0.0029	-0.0520	93.4	0.5408 (0.0184)	0.5410 (0.0192)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.5701 (0.0146)	0.5623 (0.0147)	0.0003	-0.0077	92.0	0.5444 (0.0107)	0.5441 (0.0105)	0.5574 (0.0141)	0.0004	-0.0126	85.2	0.5408 (0.0102)	0.5407 (0.0102)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity SE)
2	0.5694 (0.0143)	0.5618 (0.0143)	0.0003	-0.0077	92.4	0.5441 (0.0106)	0.5436 (0.0105)	0.5571 (0.0138)	0.0003	-0.0124	85.4	0.5405 (0.0100)	0.5404 (0.0101)
3	0.5677 (0.0139)	0.5601 (0.0139)	0.0002	-0.0076	92.4	0.5430 (0.0109)	0.5425 (0.0104)	0.5560 (0.0136)	0.0003	-0.0117	86.0	0.5399 (0.0106)	0.5397 (0.0101)
4	0.5626 (0.0154)	0.5552 (0.0144)	0.0003	-0.0074	93.4	0.5402 (0.0181)	0.5390 (0.0187)	0.5523 (0.0147)	0.0003	-0.0103	90.0	0.5376 (0.0177)	0.5376 (0.0190)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.5701 (0.0146)	0.5587 (0.0151)	0.0004	-0.0114	87.8	0.5417 (0.0112)	0.5415 (0.0107)	0.5498 (0.0142)	0.0006	-0.0203	70.0	0.5353 (0.0101)	0.5353 (0.0103)
2	0.5694 (0.0143)	0.5583 (0.0148)	0.0003	-0.0111	87.6	0.5415 (0.0109)	0.5412 (0.0107)	0.5495 (0.0140)	0.0006	-0.0199	70.2	0.5352 (0.0101)	0.5350 (0.0102)
3	0.5677 (0.0139)	0.5566 (0.0142)	0.0003	-0.0111	87.0	0.5406 (0.0110)	0.5399 (0.0107)	0.5487 (0.0137)	0.0005	-0.0190	70.6	0.5348 (0.0184)	0.5344 (0.0103)
4	0.5626 (0.0154)	0.5515 (0.0141)	0.0003	-0.0111	88.4	0.5374 (0.0183)	0.5366 (0.0177)	0.5458 (0.0145)	0.0005	-0.0168	76.8	0.5329 (0.0184)	0.5330 (0.0186)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.5701 (0.0146)	0.5561 (0.0155)	0.0004	-0.0140	83.8	0.5400 (0.0113)	0.5397 (0.0111)	0.5446 (0.0143)	0.0009	-0.0255	59.4	0.5361 (0.0102)	0.5316 (0.0103)
2	0.5694 (0.0143)	0.5561 (0.0152)	0.0004	-0.0133	84.8	0.5399 (0.0112)	0.5397 (0.0110)	0.5443 (0.0141)	0.0008	-0.0251	59.2	0.5315 (0.0102)	0.5314 (0.0102)
3	0.5677 (0.0139)	0.5544 (0.0145)	0.0004	-0.0132	84.0	0.5387 (0.0112)	0.5387 (0.0108)	0.5437 (0.0139)	0.0008	-0.0239	60.8	0.5310 (0.0103)	0.5311 (0.0104)
4	0.5626 (0.0154)	0.5494 (0.0141)	0.0004	-0.0132	84.2	0.5364 (0.0180)	0.5345 (0.0176)	0.5412 (0.0144)	0.0007	-0.0214	66.4	0.5295 (0.0181)	0.5298 (0.0187)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5701 (0.0146)	0.5542 (0.0156)	0.0005	-0.0159	81.0	0.5386 (0.0115)	0.5382 (0.0111)	0.5407 (0.0143)	0.0011	-0.0294	47.8	0.5290 (0.0103)	0.5288 (0.0103)
2	0.5694 (0.0143)	0.5545 (0.0154)	0.0005	-0.0150	82.4	0.5387 (0.0114)	0.5386 (0.0110)	0.5406 (0.0142)	0.0010	-0.0289	49.2	0.5288 (0.0102)	0.5287 (0.0103)
3	0.5677 (0.0139)	0.5529 (0.0148)	0.0004	-0.0147	81.6	0.5379 (0.0113)	0.5373 (0.0178)	0.5401 (0.0140)	0.0010	-0.0276	52.0	0.5284 (0.0106)	0.5285 (0.0103)
4	0.5626 (0.0154)	0.5479 (0.0141)	0.0004	-0.0147	79.8	0.5349 (0.0180)	0.5339 (0.0178)	0.5379 (0.0143)	0.0008	-0.0247	58.4	0.5275 (0.0177)	0.5269 (0.0183)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.5701 (0.0146)	0.5525 (0.0158)	0.0006	-0.0175	78.8	0.5375 (0.0116)	0.5370 (0.0111)	0.5378 (0.0144)	0.0013	-0.0323	38.0	0.5269 (0.0103)	0.5267 (0.0103)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity SE)
2	0.5694 (0.0143)	0.5531 (0.0157)	0.0005	-0.0163	80.2	0.5378 (0.0116)	0.5376 (0.0112)	0.5376 (0.0143)	0.0012	-0.0318	39.4	0.5268 (0.0103)	0.5266 (0.0102)
3	0.5677 (0.0139)	0.5517 (0.0150)	0.0005	-0.0159	80.4	0.5370 (0.0115)	0.5366 (0.0111)	0.5372 (0.0140)	0.0011	-0.0305	41.8	0.5268 (0.0104)	0.5260 (0.0104)
4	0.5626 (0.0154)	0.5467 (0.0141)	0.0005	-0.0159	79.0	0.5346 (0.0176)	0.5325 (0.0180)	0.5352 (0.0143)	0.0010	-0.0274	50.6	0.5264 (0.0180)	0.5242 (0.0179)

Table S9: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 0.5$ and 30% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.6366 (0.0154)	0.6267 (0.0154)	0.0003	-0.0099	90.2	0.5908 (0.0115)	0.5900 (0.0117)	0.6194 (0.0147)	0.0005	-0.0172	79.8	0.5853 (0.0110)	0.5851 (0.0110)
2	0.6324 (0.0144)	0.6225 (0.0143)	0.0003	-0.0099	89.2	0.5884 (0.0113)	0.5865 (0.0110)	0.6166 (0.0138)	0.0004	-0.0158	79.4	0.5836 (0.0108)	0.5827 (0.0105)
3	0.6239 (0.0133)	0.6143 (0.0130)	0.0003	-0.0096	89.4	0.5832 (0.0112)	0.5802 (0.0108)	0.6107 (0.0130)	0.0003	-0.0132	83.4	0.5801 (0.0111)	0.5780 (0.0107)
4	0.6096 (0.0174)	0.6001 (0.0164)	0.0004	-0.0095	91.2	0.5732 (0.0183)	0.5705 (0.0198)	0.5996 (0.0143)	0.0003	-0.0100	90.2	0.5726 (0.0186)	0.5709 (0.0200)
Measurement error $\sigma_e^2 = 0.5$													
1	0.6366 (0.0154)	0.6214 (0.0160)	0.0005	-0.0152	83.4	0.5869 (0.0120)	0.5863 (0.0120)	0.6073 (0.0146)	0.0011	-0.0293	48.8	0.5767 (0.0108)	0.5763 (0.0109)
2	0.6324 (0.0144)	0.6172 (0.0147)	0.0004	-0.0152	81.4	0.5843 (0.0114)	0.5829 (0.0111)	0.6052 (0.0138)	0.0009	-0.0272	51.4	0.5753 (0.0105)	0.5747 (0.0105)
3	0.6239 (0.0133)	0.6088 (0.0132)	0.0004	-0.0151	80.0	0.5793 (0.0111)	0.5761 (0.0111)	0.6008 (0.0131)	0.0007	-0.0231	58.0	0.5724 (0.0112)	0.5714 (0.0103)
4	0.6096 (0.0174)	0.5945 (0.0158)	0.0005	-0.0151	83.8	0.5694 (0.0171)	0.5661 (0.0184)	0.5918 (0.0161)	0.0006	-0.0178	80.0	0.5670 (0.0190)	0.5653 (0.0186)
Measurement error $\sigma_e^2 = 1.0$													
1	0.6366 (0.0154)	0.6147 (0.0170)	0.0008	-0.0220	74.2	0.5821 (0.0128)	0.5814 (0.0124)	0.5913 (0.0146)	0.0023	-0.0454	13.0	0.5652 (0.0108)	0.5647 (0.0108)
2	0.6324 (0.0144)	0.6109 (0.0155)	0.0007	-0.0215	71.0	0.5797 (0.0120)	0.5785 (0.0117)	0.5899 (0.0141)	0.0020	-0.0425	14.6	0.5642 (0.0106)	0.5638 (0.0105)
3	0.6239 (0.0133)	0.6024 (0.0137)	0.0006	-0.0215	68.4	0.5744 (0.0115)	0.5781 (0.0111)	0.5870 (0.0135)	0.0015	-0.0369	23.6	0.5622 (0.0108)	0.5617 (0.0107)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
4	0.6096 (0.0174)	0.5881 (0.0152)	0.0007	-0.0215	68.2	0.5645 (0.0170)	0.5618 (0.0180)	0.5804 (0.0155)	0.0011	-0.0292	51.2	0.5591 (0.0172)	0.5567 (0.0173)
Measurement error $\sigma_e^2 = 1.5$													
1	0.6366 (0.0154)	0.6101 (0.0177)	0.0010	-0.0265	67.0	0.5789 (0.0134)	0.5780 (0.0129)	0.5808 (0.0147)	0.0033	-0.0558	3.6	0.5576 (0.0108)	0.5573 (0.0107)
2	0.6324 (0.0144)	0.6071 (0.0162)	0.0009	-0.0254	66.2	0.5771 (0.0126)	0.5756 (0.0119)	0.5798 (0.0142)	0.0030	-0.0526	4.8	0.5571 (0.0106)	0.5565 (0.0105)
3	0.6239 (0.0133)	0.5988 (0.0142)	0.0008	-0.0251	58.4	0.5717 (0.0118)	0.5692 (0.0112)	0.5776 (0.0137)	0.0023	-0.0463	8.2	0.5554 (0.0107)	0.5551 (0.0108)
4	0.6096 (0.0174)	0.5845 (0.0150)	0.0009	-0.0251	59.0	0.5617 (0.0178)	0.5595 (0.0174)	0.5724 (0.0152)	0.0016	-0.0372	33.4	0.5525 (0.0165)	0.5516 (0.0166)
Measurement error $\sigma_e^2 = 2.0$													
1	0.6366 (0.0154)	0.6064 (0.0183)	0.0012	-0.0302	62.4	0.5764 (0.0138)	0.5753 (0.0133)	0.5733 (0.0147)	0.0042	-0.0633	1.0	0.5522 (0.0109)	0.5520 (0.0106)
2	0.6324 (0.0144)	0.6042 (0.0168)	0.0011	-0.0283	61.4	0.5749 (0.0128)	0.5735 (0.0124)	0.5726 (0.0143)	0.0042	-0.0633	1.8	0.5517 (0.0107)	0.5514 (0.0105)
3	0.6239 (0.0133)	0.5962 (0.0147)	0.0010	-0.0277	54.2	0.5699 (0.0122)	0.5673 (0.0112)	0.5708 (0.0138)	0.0038	-0.0599	2.6	0.5504 (0.0106)	0.5503 (0.0108)
4	0.6096 (0.0174)	0.5821 (0.0150)	0.0010	-0.0275	52.6	0.5603 (0.0180)	0.5574 (0.0164)	0.5664 (0.0150)	0.0030	-0.0531	18.4	0.5480 (0.0165)	0.5474 (0.0168)
Measurement error $\sigma_e^2 = 2.5$													
1	0.6366 (0.0154)	0.6033 (0.0188)	0.0015	-0.0333	55.8	0.5745 (0.0141)	0.5727 (0.0136)	0.5676 (0.0147)	0.0050	-0.0691	0.2	0.5480 (0.0107)	0.5480 (0.0107)
2	0.6324 (0.0144)	0.6017 (0.0173)	0.0012	-0.0308	58.0	0.5732 (0.0133)	0.5717 (0.0126)	0.5670 (0.0144)	0.0045	-0.0655	0.6	0.5476 (0.0106)	0.5476 (0.0105)
3	0.6239 (0.0133)	0.5942 (0.0151)	0.0011	-0.0297	49.0	0.5685 (0.0126)	0.5658 (0.0161)	0.5655 (0.0139)	0.0036	-0.0584	0.8	0.5498 (0.0107)	0.5464 (0.0106)
4	0.6096 (0.0174)	0.5804 (0.0151)	0.0011	-0.0292	47.2	0.5588 (0.0182)	0.5564 (0.0161)	0.5617 (0.0148)	0.0025	-0.0480	11.0	0.5438 (0.0167)	0.5447 (0.0168)

Table S10: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 0.75$ and 30% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.6955 (0.0153)	0.6815 (0.0161)	0.0005	-0.0141	86.2	0.6320 (0.0125)	0.6297 (0.0129)	0.6673 (0.0149)	0.0010	-0.0282	53.6	0.6211 (0.0115)	0.6197 (0.0118)
2	0.6839 (0.0145)	0.6694 (0.0145)	0.0004	-0.0145	83.4	0.6248 (0.0121)	0.6195 (0.0117)	0.6597 (0.0138)	0.0008	-0.0242	59.0	0.6162 (0.0114)	0.6134 (0.0111)
3	0.6677 (0.0136)	0.6531 (0.0134)	0.0004	-0.0147	83.0	0.6138 (0.0120)	0.6067 (0.0115)	0.6487 (0.0131)	0.0005	-0.0190	71.0	0.6085 (0.0118)	0.6054 (0.0118)
4	0.6468 (0.0182)	0.6318 (0.0172)	0.0005	-0.0150	85.2	0.5984 (0.0180)	0.5913 (0.0195)	0.6335 (0.0177)	0.0005	-0.0133	88.8	0.5992 (0.0174)	0.5934 (0.0192)
Measurement error $\sigma_e^2 = 0.5$													
1	0.6955 (0.0153)	0.6742 (0.0172)	0.0007	-0.0213	76.2	0.6268 (0.0135)	0.6243 (0.0133)	0.6485 (0.0150)	0.0024	-0.0471	12.0	0.6069 (0.0114)	0.6061 (0.0117)
2	0.6839 (0.0145)	0.6621 (0.0152)	0.0007	-0.0218	70.4	0.6192 (0.0125)	0.6142 (0.0120)	0.6429 (0.0139)	0.0019	-0.0410	14.4	0.6035 (0.0108)	0.6015 (0.0112)
3	0.6677 (0.0136)	0.6454 (0.0136)	0.0007	-0.0223	62.6	0.6085 (0.0121)	0.6009 (0.011)	0.6348 (0.0133)	0.0013	-0.0329	31.6	0.5979 (0.0114)	0.5955 (0.0116)
4	0.6468 (0.0182)	0.6239 (0.0165)	0.0008	-0.0228	70.6	0.5933 (0.0174)	0.5913 (0.0179)	0.6231 (0.0167)	0.0008	-0.0236	70.8	0.5902 (0.0167)	0.5873 (0.0186)
Measurement error $\sigma_e^2 = 1.0$													
1	0.6955 (0.0153)	0.6651 (0.0189)	0.0013	-0.0304	63.0	0.6201 (0.0149)	0.6175 (0.0142)	0.6244 (0.0151)	0.0053	-0.0711	0.4	0.5893 (0.0112)	0.5885 (0.0116)
2	0.6839 (0.0145)	0.6539 (0.0164)	0.0012	-0.0300	56.2	0.6131 (0.0133)	0.6081 (0.0126)	0.6209 (0.0142)	0.0042	-0.0630	0.4	0.5870 (0.0108)	0.5858 (0.0110)
3	0.6677 (0.0136)	0.6371 (0.0142)	0.0011	-0.0307	42.6	0.6020 (0.0125)	0.5950 (0.0117)	0.6158 (0.0136)	0.0029	-0.0519	4.0	0.5835 (0.0112)	0.5822 (0.0113)
4	0.6468 (0.0182)	0.6154 (0.0156)	0.0012	-0.0314	45.8	0.5865 (0.0175)	0.5793 (0.0173)	0.6078 (0.0156)	0.0018	-0.0389	29.6	0.5791 (0.0159)	0.5761 (0.0173)
Measurement error $\sigma_e^2 = 1.5$													
1	0.6955 (0.0153)	0.6589 (0.0203)	0.0018	-0.0366	55.2	0.6158 (0.0159)	0.6127 (0.0150)	0.6092 (0.0151)	0.0077	-0.0863	0.0	0.5781 (0.0112)	0.5776 (0.0114)
2	0.6839 (0.0145)	0.6489 (0.0175)	0.0015	-0.0350	48.6	0.6094 (0.0143)	0.6044 (0.0130)	0.6068 (0.0144)	0.0062	-0.0771	0.0	0.5765 (0.0109)	0.5758 (0.0109)
3	0.6677 (0.0136)	0.6324 (0.0148)	0.0015	-0.0353	34.0	0.5986 (0.0131)	0.5917 (0.0118)	0.6031 (0.0138)	0.0044	-0.0647	0.6	0.5739 (0.0112)	0.5733 (0.0112)
4	0.6468 (0.0182)	0.6108 (0.0154)	0.0015	-0.0360	35.2	0.5834 (0.0172)	0.5758 (0.0170)	0.5970 (0.0151)	0.0027	-0.0497	9.8	0.5706 (0.0154)	0.5688 (0.0166)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.6955 (0.0153)	0.6540 (0.0214)	0.0022	-0.0416	48.2	0.6125 (0.0168)	0.6087 (0.0156)	0.5985 (0.0151)	0.0096	-0.0970	0.0	0.5705 (0.0112)	0.5699 (0.0112)
2	0.6839 (0.0145)	0.6451 (0.0185)	0.0018	-0.0388	43.6	0.6067 (0.0149)	0.6017 (0.0137)	0.5967 (0.0145)	0.0078	-0.0872	0.0	0.5692 (0.0109)	0.5686 (0.0109)
3	0.6677 (0.0136)	0.6293 (0.0154)	0.0017	-0.0384	29.4	0.5963 (0.0134)	0.5893 (0.0121)	0.5938 (0.0139)	0.0057	-0.0739	0.0	0.5672 (0.0114)	0.5666 (0.0110)
4	0.6468 (0.0182)	0.6079 (0.0153)	0.0017	-0.0389	28.8	0.5829 (0.0172)	0.5721 (0.0162)	0.5889 (0.0148)	0.0036	-0.0579	3.2	0.5644 (0.0147)	0.5631 (0.0155)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.6955 (0.0152)	0.6495 (0.0224)	0.0026	-0.0459	44.4	0.6096 (0.0174)	0.6052 (0.0163)	0.5906 (0.0151)	0.0112	-0.1049	0.0	0.5646 (0.0111)	0.5643 (0.0111)
2	0.6839 (0.0145)	0.6419 (0.0193)	0.0021	-0.0420	38.8	0.6044 (0.0155)	0.5991 (0.0140)	0.5891 (0.0145)	0.0092	-0.0948	0.0	0.5636 (0.0108)	0.5632 (0.0109)
3	0.6678 (0.0136)	0.6269 (0.0159)	0.0019	-0.0409	27.4	0.5944 (0.0140)	0.5875 (0.0124)	0.5868 (0.0140)	0.0068	-0.0810	0.0	0.5620 (0.0112)	0.5617 (0.0109)
4	0.6468 (0.0182)	0.6058 (0.0155)	0.0019	-0.0410	24.4	0.5810 (0.0179)	0.5710 (0.0154)	0.5826 (0.0145)	0.0043	-0.0641	1.0	0.5593 (0.0144)	0.5591 (0.0151)

Table S11: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 1.0 and 30% censoring

t_h	True AUC (SE)	Measurement-error Adjusted						Observed biomarker					
		AUC(SE)	MSE	Bias	Cov	Sensitivity	Specificity	AUC(SE)	MSE	Bias	Cov	Sensitivity	Specificity
Measurement error $\sigma_e^2 =$ 0.25													
1	0.7433 (0.0148)	0.7256 (0.0160)	0.0006	-0.0176	81.0	0.6676 (0.0132)	0.6620 (0.0134)	0.7045 (0.0152)	0.0017	-0.0388	27.4	0.6499 (0.0120)	0.6470 (0.0127)
2	0.7230 (0.0139)	0.7046 (0.0143)	0.0005	-0.0184	75.8	0.6538 (0.0125)	0.6439 (0.0121)	0.6915 (0.0138)	0.0012	-0.0315	36.2	0.6413 (0.0115)	0.6361 (0.0117)
3	0.7007 (0.0139)	0.6816 (0.0136)	0.0005	-0.0191	70.6	0.6380 (0.0128)	0.6253 (0.0122)	0.6767 (0.0135)	0.0008	-0.0240	57.0	0.6306 (0.0122)	0.6248 (0.0128)
4	0.6769 (0.0195)	0.6570 (0.0181)	0.0007	-0.0199	79.8	0.6202 (0.0190)	0.6067 (0.0184)	0.6599 (0.0185)	0.0006	-0.0170	84.4	0.6191 (0.0173)	0.6123 (0.0201)
Measurement error $\sigma_e^2 =$ 0.5													

1	0.7433 (0.0148)	0.7171 (0.0173)	0.0010	-0.0262	67.0	0.6609 (0.0142)	0.6554 (0.0139)	0.6797 (0.0154)	0.0043	-0.0635	1.8	0.6308 (0.0119)	0.6287 (0.0126)
2	0.7230 (0.0139)	0.6960 (0.0150)	0.0010	-0.0270	57.6	0.6471 (0.0132)	0.6374 (0.0123)	0.6705 (0.0141)	0.0030	-0.0525	4.4	0.6247 (0.0114)	0.6210 (0.0115)
3	0.7007 (0.0139)	0.6726 (0.0138)	0.0010	-0.0281	47.0	0.6312 (0.0132)	0.6187 (0.0121)	0.6597 (0.0136)	0.0019	-0.0410	13.2	0.6172 (0.0120)	0.6128 (0.0122)
4	0.6769 (0.0195)	0.6475 (0.0173)	0.0012	-0.0294	60.2	0.6125 (0.0182)	0.6002 (0.0171)	0.6470 (0.0172)	0.0012	-0.0299	58.4	0.6088 (0.0165)	0.6035 (0.0180)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.7433 (0.0148)	0.7062 (0.0192)	0.0017	-0.0370	49.8	0.6530 (0.0158)	0.6470 (0.0149)	0.6490 (0.0157)	0.0091	-0.0943	0.0	0.6076 (0.0119)	0.6062 (0.0122)
2	0.7230 (0.0139)	0.6866 (0.0165)	0.0016	-0.0364	39.0	0.6399 (0.0143)	0.6305 (0.0129)	0.6434 (0.0145)	0.0066	-0.0796	0.0	0.6037 (0.0113)	0.6019 (0.0115)
3	0.7007 (0.0139)	0.6633 (0.0146)	0.0016	-0.0374	27.8	0.6242 (0.0136)	0.611 (0.0122)	0.6366 (0.0138)	0.0043	-0.0641	0.4	0.5989 (0.0117)	0.5970 (0.0121)
4	0.6769 (0.0195)	0.6375 (0.0166)	0.0018	-0.0394	35.2	0.6058 (0.0174)	0.5923 (0.0164)	0.6281 (0.0158)	0.0026	-0.0488	14.6	0.5937 (0.0157)	0.5909 (0.0160)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.7433 (0.0148)	0.6987 (0.0209)	0.0024	-0.0445	43.4	0.6477 (0.0174)	0.6408 (0.0157)	0.6301 (0.0157)	0.0130	-0.1132	0.0	0.5935 (0.0118)	0.5926 (0.0120)
2	0.7230 (0.0139)	0.6809 (0.0178)	0.0021	-0.0421	32.4	0.6358 (0.0152)	0.6259 (0.0136)	0.6262 (0.0147)	0.0096	-0.0968	0.0	0.5910 (0.0113)	0.5896 (0.0115)
3	0.7007 (0.0139)	0.6583 (0.0154)	0.0020	-0.0424	21.8	0.6203 (0.0141)	0.6082 (0.0126)	0.6213 (0.0140)	0.0065	-0.0793	0.0	0.5873 (0.0117)	0.5863 (0.0117)
4	0.6769 (0.0195)	0.6324 (0.0164)	0.0022	-0.0445	21.6	0.6020 (0.0177)	0.5886 (0.0157)	0.6150 (0.0152)	0.0041	-0.0619	1.8	0.5840 (0.0144)	0.5812 (0.0165)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.7433 (0.0148)	0.6925 (0.0221)	0.0031	-0.0508	35.4	0.6436 (0.0183)	0.6357 (0.0164)	0.6170 (0.0157)	0.0162	-0.1263	0.0	0.5840 (0.0118)	0.5831 (0.0117)
2	0.7230 (0.0139)	0.6764 (0.0188)	0.0025	-0.0466	30.2	0.6323 (0.0159)	0.6226 (0.0141)	0.6226 (0.0141)	0.0121	-0.1089	0.0	0.5819 (0.0112)	0.5810 (0.0114)
3	0.7007 (0.0139)	0.6547 (0.0161)	0.0024	-0.0460	19.4	0.6173 (0.0147)	0.6058 (0.0127)	0.6058 (0.0127)	0.0084	-0.0904	0.0	0.5791 (0.0115)	0.5785 (0.0116)
4	0.6770 (0.0194)	0.6291 (0.0164)	0.0026	-0.0478	16.0	0.6001 (0.0179)	0.5859 (0.0152)	0.5859 (0.0152)	0.0054	-0.0718	1.0	0.5763 (0.0140)	0.5746 (0.0150)

Measurement error $\sigma_e^2 =$ 2.5													
1	0.7433 (0.0148)	0.6971 (0.0232)	0.0037	-0.0562	30.2	0.6397 (0.0193)	0.6315 (0.0170)	0.6073 (0.0157)	0.0187	-0.1360	0.0	0.5770 (0.0117)	0.5762 (0.0116)
2	0.7230 (0.0139)	0.6725 (0.0197)	0.0029	-0.0505	27.2	0.6297 (0.0167)	0.6193 (0.0146)	0.6050 (0.0149)	0.0142	-0.1180	0.0	0.5752 (0.0112)	0.5745 (0.0114)
3	0.7006 (0.0141)	0.6520 (0.0168)	0.0027	-0.0487	17.8	0.6154 (0.0154)	0.6035 (0.0128)	0.6019 (0.0143)	0.0100	-0.0987	0.0	0.5732 (0.0114)	0.5722 (0.0118)
4	0.6768 (0.0194)	0.6268 (0.0164)	0.0028	-0.0500	14.0	0.5992 (0.0180)	0.5835 (0.0152)	0.5976 (0.0148)	0.0065	-0.0792	0.0	0.5704 (0.0141)	0.5695 (0.0149)

Table S12: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0 and 50% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.5138 (0.0104)	0.5134 (0.0107)	0.0001	-0.0005	94.6	0.5094 (0.0743)	0.5095 (0.0076)	0.5133 (0.0102)	0.0001	-0.0005	95.6	0.5095 (0.0073)	0.5094 (0.0073)
2	0.5138 (0.0103)	0.5134 (0.0107)	0.0001	-0.0004	95.0	0.5094 (0.0079)	0.5096 (0.0075)	0.5133 (0.0102)	0.0001	-0.0005	95.6	0.5094 (0.0073)	0.5095 (0.0074)
3	0.5137 (0.0103)	0.5133 (0.0105)	0.0001	-0.0004	95.2	0.5094 (0.0088)	0.5094 (0.0077)	0.5133 (0.0102)	0.0001	-0.0004	95.6	0.5094 (0.0087)	0.5094 (0.0074)
4	0.5126 (0.0097)	0.5123 (0.0102)	0.0001	-0.0003	95.0	0.4936 (0.0298)	0.5242 (0.0264)	0.5121 (0.0098)	0.0001	-0.0004	94.6	0.4935 (0.0297)	0.5241 (0.0263)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.5140 (0.0103)	0.5136 (0.0105)	0.0001	-0.0004	95.4	0.5097 (0.0742)	0.5096 (0.0074)	0.5134 (0.0100)	0.0001	-0.0006	95.6	0.5095 (0.0071)	0.5095 (0.0072)
2	0.5130 (0.0102)	0.5136 (0.0104)	0.0001	-0.0004	95.4	0.5096 (0.0075)	0.5096 (0.0075)	0.5134 (0.0100)	0.0001	-0.0006	95.6	0.5094 (0.0073)	0.5095 (0.0073)
3	0.5139 (0.0102)	0.5135 (0.0103)	0.0001	-0.0004	95.6	0.5094 (0.0083)	0.5097 (0.0080)	0.5133 (0.0100)	0.0001	-0.0006	95.6	0.5092 (0.0084)	0.5098 (0.0075)
4	0.5128 (0.0098)	0.5125 (0.0098)	0.0001	-0.0003	95.4	0.4936 (0.0299)	0.5245 (0.0264)	0.5122 (0.0097)	0.0001	-0.0006	94.6	0.4933 (0.0299)	0.5244 (0.0263)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.5140 (0.0103)	0.5137 (0.0103)	0.0001	-0.0003	95.0	0.5097 (0.0742)	0.5097 (0.0074)	0.5134 (0.0099)	0.0001	-0.0006	95.4	0.5094 (0.0070)	0.5096 (0.0071)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.5130 (0.0102)	0.5138 (0.0105)	0.0001	-0.0002	95.4	0.5098 (0.0077)	0.5096 (0.0076)	0.5134 (0.0100)	0.0001	-0.0006	95.8	0.5094 (0.0072)	0.5095 (0.0071)
3	0.5139 (0.0102)	0.5136 (0.0103)	0.0001	-0.0003	95.4	0.5093 (0.0082)	0.5100 (0.0079)	0.5133 (0.0098)	0.0001	-0.0006	96.2	0.5093 (0.0082)	0.5096 (0.0073)
4	0.5128 (0.0098)	0.5125 (0.0102)	0.0001	-0.0002	94.6	0.4937 (0.0297)	0.5245 (0.0264)	0.5121 (0.0095)	0.0001	-0.0006	95.8	0.4932 (0.0298)	0.5244 (0.0263)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.5144 (0.0105)	0.5138 (0.0108)	0.0001	-0.0006	95.0	0.5098 (0.0755)	0.5097 (0.0077)	0.5141 (0.0100)	0.0001	-0.0003	96.0	0.5099 (0.0071)	0.5100 (0.0071)
2	0.5143 (0.0104)	0.5139 (0.0109)	0.0001	-0.0004	95.6	0.5097 (0.0080)	0.5100 (0.0077)	0.5140 (0.0099)	0.0001	-0.0003	95.4	0.5098 (0.0071)	0.5101 (0.0073)
3	0.5142 (0.0103)	0.5138 (0.0106)	0.0001	-0.0005	94.8	0.5095 (0.0084)	0.5100 (0.0082)	0.5140 (0.0099)	0.0001	-0.0003	96.0	0.5097 (0.0080)	0.5101 (0.0076)
4	0.5130 (0.0097)	0.5126 (0.0103)	0.0001	-0.0004	94.0	0.4941 (0.0299)	0.5243 (0.0266)	0.5126 (0.0093)	0.0001	-0.0004	96.0	0.4940 (0.0299)	0.5243 (0.0266)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5142 (0.0111)	0.5137 (0.0111)	0.0001	-0.0005	95.0	0.5097 (0.0706)	0.5096 (0.0079)	0.5142 (0.0105)	0.0001	0.0001	95.2	0.5101 (0.0076)	0.5100 (0.0074)
2	0.5141 (0.0111)	0.5139 (0.0113)	0.0001	-0.0002	95.0	0.5098 (0.0082)	0.5098 (0.0080)	0.5142 (0.0105)	0.0001	0.0001	95.2	0.5100 (0.0075)	0.5101 (0.0077)
3	0.5139 (0.0108)	0.5137 (0.0111)	0.0001	-0.0002	94.6	0.5094 (0.0092)	0.5101 (0.0081)	0.5140 (0.0103)	0.0001	0.0001	95.2	0.5098 (0.0082)	0.5101 (0.0081)
4	0.5128 (0.0105)	0.5126 (0.0106)	0.0001	-0.0002	94.8	0.4942 (0.0298)	0.5241 (0.0257)	0.5130 (0.0103)	0.0001	0.0002	95.4	0.4947 (0.0288)	0.5241 (0.0257)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.5138 (0.0104)	0.5135 (0.0105)	0.0001	-0.0003	94.8	0.5096 (0.0696)	0.5095 (0.0074)	0.5137 (0.0102)	0.0001	-0.0001	96.6	0.5097 (0.0073)	0.5097 (0.0073)
2	0.5137 (0.0104)	0.5138 (0.0107)	0.0001	0.0001	94.6	0.5096 (0.0077)	0.5100 (0.0077)	0.5146 (0.0102)	0.0001	-0.0001	96.6	0.5096 (0.0074)	0.5097 (0.0073)
3	0.5136 (0.0103)	0.5138 (0.0106)	0.0001	0.0003	94.2	0.5094 (0.0089)	0.5102 (0.0079)	0.5135 (0.0099)	0.0001	-0.0001	96.6	0.5093 (0.0081)	0.5098 (0.0077)
4	0.5123 (0.0096)	0.5126 (0.0099)	0.0001	0.0003	94.2	0.4931 (0.0319)	0.5253 (0.0253)	0.5122 (0.0095)	0.0001	-0.0002	96.6	0.4925 (0.0310)	0.5251 (0.0288)

Table S13: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0.25 and 50% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.5693 (0.0176)	0.5642 (0.0172)	0.0003	-0.0052	93.6	0.5455 (0.0125)	0.5456 (0.0124)	0.5613 (0.0170)	0.0004	-0.0080	91.4	0.5435 (0.0122)	0.5436 (0.0124)
2	0.5686 (0.0174)	0.5635 (0.0170)	0.0003	-0.0051	93.8	0.5453 (0.0127)	0.5448 (0.0122)	0.5608 (0.0168)	0.1025	-0.3198	91.4	0.5433 (0.0123)	0.5430 (0.0124)
3	0.5677 (0.0167)	0.5618 (0.0164)	0.0003	-0.0049	93.8	0.5440 (0.0124)	0.5438 (0.0129)	0.5594 (0.0164)	0.0003	-0.0073	92.2	0.5427 (0.0129)	0.5418 (0.0129)
4	0.5591 (0.0179)	0.5542 (0.0167)	0.0003	-0.0049	94.4	0.5400 (0.0296)	0.5388 (0.0287)	0.5525 (0.0169)	0.0003	-0.0065	93.6	0.5399 (0.0294)	0.5365 (0.0282)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.5693 (0.0176)	0.5614 (0.0174)	0.0004	-0.0080	92.0	0.5435 (0.0125)	0.5436 (0.0127)	0.5556 (0.0169)	0.0005	-0.0137	86.8	0.5395 (0.0122)	0.5395 (0.0123)
2	0.5686 (0.0174)	0.5608 (0.0172)	0.0004	-0.0078	91.6	0.5432 (0.0126)	0.5431 (0.0125)	0.5552 (0.0167)	0.0005	-0.0134	86.6	0.5393 (0.0124)	0.5391 (0.0121)
3	0.5677 (0.0167)	0.5589 (0.0165)	0.0003	-0.0078	92.2	0.5420 (0.0127)	0.5417 (0.0127)	0.5541 (0.0164)	0.0004	-0.0126	88.2	0.5386 (0.0127)	0.5383 (0.0130)
4	0.5591 (0.0179)	0.5514 (0.0163)	0.0003	-0.0077	93.0	0.5371 (0.0288)	0.5375 (0.0287)	0.5481 (0.0167)	0.0004	-0.0110	90.8	0.5356 (0.0296)	0.5342 (0.0282)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.5693 (0.0176)	0.5577 (0.0179)	0.0005	-0.0117	90.2	0.5409 (0.0130)	0.5410 (0.0128)	0.5478 (0.0169)	0.0008	-0.0216	75.0	0.5338 (0.0121)	0.5339 (0.0122)
2	0.5686 (0.0174)	0.5574 (0.0176)	0.0004	-0.0112	89.8	0.5409 (0.0131)	0.5405 (0.0126)	0.5475 (0.0168)	0.1025	-0.3198	76.6	0.5336 (0.0121)	0.5338 (0.0122)
3	0.5677 (0.0167)	0.5554 (0.0168)	0.0004	-0.0112	89.8	0.5392 (0.0129)	0.5394 (0.0128)	0.5467 (0.0164)	0.0007	-0.0200	77.7	0.5335 (0.0127)	0.5328 (0.0127)
4	0.5591 (0.0179)	0.5479 (0.0160)	0.0004	-0.0112	89.0	0.5353 (0.0291)	0.5343 (0.0282)	0.5418 (0.0166)	0.0006	-0.0173	81.6	0.5323 (0.0290)	0.5282 (0.0267)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.5693 (0.0176)	0.5551 (0.0182)	0.0005	-0.0143	64.2	0.5391 (0.0132)	0.5390 (0.0130)	0.5425 (0.0170)	0.0010	-0.0268	88.0	0.5300 (0.0120)	0.5302 (0.0123)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.5686 (0.0174)	0.5552 (0.0181)	0.0005	-0.0134	65.2	0.5392 (0.0132)	0.5392 (0.0130)	0.5423 (0.0168)	0.0010	-0.0263	88.0	0.5300 (0.0120)	0.5300 (0.0124)
3	0.5677 (0.0167)	0.5533 (0.0172)	0.0005	-0.0133	67.2	0.5377 (0.0134)	0.5380 (0.0129)	0.5417 (0.0165)	0.0009	-0.0250	88.2	0.5295 (0.0125)	0.5297 (0.0126)
4	0.5591 (0.0179)	0.5459 (0.0160)	0.0004	-0.0132	73.4	0.5343 (0.0292)	0.5343 (0.0275)	0.5374 (0.0165)	0.0007	-0.0217	86.4	0.5278 (0.0291)	0.5264 (0.0258)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5693 (0.0176)	0.5530 (0.0184)	0.0006	-0.0163	85.4	0.5377 (0.0133)	0.5375 (0.0132)	0.5386 (0.0170)	0.0012	-0.0307	53.8	0.5273 (0.0120)	0.5275 (0.0123)
2	0.5686 (0.0174)	0.5536 (0.0184)	0.0006	-0.0150	86.4	0.5380 (0.0134)	0.5380 (0.0132)	0.5385 (0.0168)	0.0012	-0.0301	55.2	0.5272 (0.0122)	0.5274 (0.0121)
3	0.5677 (0.0167)	0.5519 (0.0175)	0.0005	-0.0148	87.2	0.5367 (0.0135)	0.5369 (0.0133)	0.5380 (0.0165)	0.0011	-0.0287	59.0	0.5268 (0.0125)	0.5271 (0.0126)
4	0.5591 (0.0179)	0.5445 (0.0161)	0.0005	-0.0146	83.8	0.5333 (0.0296)	0.5313 (0.0272)	0.5342 (0.0165)	0.0009	-0.0249	64.2	0.5242 (0.0290)	0.5253 (0.0254)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.5693 (0.0176)	0.5513 (0.0185)	0.0007	-0.0181	84.0	0.5364 (0.0135)	0.5363 (0.0131)	0.5358 (0.0169)	0.0014	-0.0336	45.8	0.5252 (0.0120)	0.5254 (0.0122)
2	0.5686 (0.0174)	0.5522 (0.0186)	0.0006	-0.0164	84.8	0.5371 (0.0136)	0.5369 (0.0134)	0.5356 (0.0167)	0.0014	-0.0330	46.8	0.5252 (0.0120)	0.5253 (0.0121)
3	0.5677 (0.0167)	0.5507 (0.0178)	0.0006	-0.0160	85.4	0.5359 (0.0136)	0.5361 (0.0135)	0.5352 (0.0164)	0.0013	-0.0315	48.6	0.5249 (0.0126)	0.5250 (0.0123)
4	0.5591 (0.0179)	0.5435 (0.0163)	0.0005	-0.0156	83.6	0.5320 (0.0293)	0.5311 (0.0271)	0.5318 (0.0163)	0.0010	-0.0273	56.6	0.5212 (0.0291)	0.5248 (0.0252)

Table S14: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0.5 and 50% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.6356 (0.0174)	0.6253 (0.0178)	0.0004	-0.0103	91.2	0.5897 (0.0135)	0.5894 (0.0133)	0.6182 (0.0171)	0.0006	-0.0174	82.2	0.5845 (0.0128)	0.5843 (0.0130)
2	0.6315 (0.0166)	0.6213 (0.0168)	0.0004	-0.0102	90.6	0.5872 (0.0131)	0.5860 (0.0128)	0.6155 (0.0165)	0.0184	-0.1347	83.0	0.5827 (0.0128)	0.5822 (0.0127)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
3	0.6223 (0.0160)	0.6121 (0.0157)	0.0004	-0.0102	90.8	0.5812 (0.0131)	0.5782 (0.0135)	0.6088 (0.0158)	0.0004	-0.0135	85.4	0.5786 (0.0134)	0.5771 (0.0139)
4	0.6062 (0.0208)	0.5966 (0.0193)	0.0005	-0.0095	92.4	0.5739 (0.0268)	0.5668 (0.0286)	0.5959 (0.0201)	0.0005	-0.0102	91.6	0.5720 (0.0269)	0.5673 (0.0272)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.6356 (0.0174)	0.6200 (0.0185)	0.0006	-0.0156	85.8	0.5856 (0.0139)	0.5858 (0.0138)	0.6062 (0.0171)	0.0012	-0.0294	59.2	0.5758 (0.0126)	0.5756 (0.0129)
2	0.6315 (0.0166)	0.6159 (0.0173)	0.0005	-0.0155	84.8	0.5832 (0.0136)	0.5823 (0.0129)	0.6042 (0.0166)	0.0184	-0.1347	61.0	0.5744 (0.0127)	0.5741 (0.0126)
3	0.6223 (0.0160)	0.6065 (0.0158)	0.0005	-0.0158	82.6	0.5774 (0.0135)	0.5749 (0.0134)	0.5989 (0.0158)	0.0008	-0.0234	65.2	0.5714 (0.0129)	0.5700 (0.0132)
4	0.6062 (0.0208)	0.5912 (0.0187)	0.0006	-0.0150	85.6	0.5697 (0.0267)	0.5629 (0.0276)	0.5883 (0.0195)	0.0007	-0.0178	84.6	0.5666 (0.0264)	0.5619 (0.0274)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.6356 (0.0174)	0.6130 (0.0196)	0.0009	-0.0226	79.6	0.5808 (0.0148)	0.5805 (0.0143)	0.5903 (0.0172)	0.0024	-0.0455	26.4	0.5641 (0.0126)	0.5642 (0.0127)
2	0.6315 (0.0166)	0.6097 (0.0183)	0.0008	-0.0218	77.4	0.5786 (0.0141)	0.5778 (0.0135)	0.5889 (0.0167)	0.0184	-0.1347	28.6	0.5631 (0.0123)	0.5633 (0.0128)
3	0.6223 (0.0160)	0.6003 (0.0164)	0.0008	-0.0220	72.0	0.5727 (0.0137)	0.5705 (0.0134)	0.5853 (0.0159)	0.0016	-0.0370	35.8	0.5611 (0.0131)	0.5606 (0.0126)
4	0.6062 (0.0208)	0.5850 (0.0181)	0.0008	-0.0212	77.2	0.5655 (0.0263)	0.5579 (0.0270)	0.5773 (0.0187)	0.0012	-0.0289	65.0	0.5580 (0.0256)	0.5543 (0.0261)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.6356 (0.0174)	0.6081 (0.0204)	0.0012	-0.0275	69.4	0.5774 (0.0153)	0.5768 (0.0148)	0.5797 (0.0173)	0.0034	-0.0559	9.8	0.5566 (0.0125)	0.5567 (0.0127)
2	0.6315 (0.0166)	0.6057 (0.0190)	0.0010	-0.0258	77.4	0.5758 (0.0149)	0.5748 (0.0137)	0.5788 (0.0169)	0.0184	-0.1347	12.8	0.5561 (0.0124)	0.5559 (0.0126)
3	0.6223 (0.0160)	0.5966 (0.0169)	0.0009	-0.0257	72.0	0.5703 (0.0145)	0.5676 (0.0137)	0.5761 (0.0161)	0.0024	-0.0462	17.6	0.5547 (0.0128)	0.5537 (0.0130)
4	0.6062 (0.0208)	0.5850 (0.0180)	0.0008	-0.0212	77.2	0.5627 (0.0260)	0.5554 (0.0270)	0.5696 (0.0182)	0.0017	-0.0366	47.4	0.5508 (0.0254)	0.5501 (0.0252)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.6356 (0.0174)	0.6041 (0.0209)	0.0014	-0.0315	66.2	0.5745 (0.0156)	0.5738 (0.0151)	0.5722 (0.0173)	0.0043	-0.0634	5.6	0.5512 (0.0125)	0.5513 (0.0127)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.6315 (0.0166)	0.6025 (0.0196)	0.0012	-0.0289	67.8	0.5735 (0.0149)	0.5727 (0.0144)	0.5714 (0.0169)	0.0184	-0.1347	6.6	0.5508 (0.0124)	0.5507 (0.0126)
3	0.6223 (0.0160)	0.5941 (0.0174)	0.0011	-0.0282	63.2	0.5688 (0.0146)	0.5655 (0.0138)	0.5693 (0.0162)	0.0031	-0.0530	10.4	0.5498 (0.0129)	0.5498 (0.0129)
4	0.6062 (0.0208)	0.5792 (0.0180)	0.0011	-0.0270	67.2	0.5602 (0.0257)	0.5545 (0.0269)	0.5638 (0.0178)	0.0021	-0.0424	31.4	0.5467 (0.0252)	0.5456 (0.0251)
Measurement error $\sigma_e^2 = 2.5$													
1	0.6356 (0.0174)	0.6006 (0.0214)	0.0017	-0.0350	62.0	0.5723 (0.0160)	0.5711 (0.0154)	0.5665 (0.0174)	0.0051	-0.0692	2.6	0.5480 (0.0107)	0.5480 (0.0107)
2	0.6315 (0.0166)	0.5999 (0.0201)	0.0014	-0.0315	64.4	0.5719 (0.0154)	0.5705 (0.0146)	0.5658 (0.0170)	0.0184	-0.1347	3.2	0.5476 (0.0106)	0.5476 (0.0105)
3	0.6223 (0.0160)	0.5921 (0.0178)	0.0012	-0.0302	61.4	0.5669 (0.0147)	0.5645 (0.0141)	0.5641 (0.0163)	0.0037	-0.0582	5.6	0.5498 (0.0107)	0.5464 (0.0106)
4	0.6062 (0.0208)	0.5776 (0.0181)	0.0011	-0.0286	64.4	0.5590 (0.0262)	0.5535 (0.0270)	0.5592 (0.0176)	0.0025	-0.0470	22.4	0.5438 (0.0167)	0.5447 (0.0168)

Table S15: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 0.75$ and 50% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.6947 (0.0176)	0.6797 (0.0187)	0.0006	-0.0150	86.4	0.6304 (0.0146)	0.6290 (0.0147)	0.6668 (0.0177)	0.0011	-0.0279	63.6	0.6206 (0.0137)	0.6195 (0.0140)
2	0.6828 (0.0159)	0.6677 (0.0164)	0.0005	-0.0151	85.0	0.6231 (0.0136)	0.6186 (0.0132)	0.6591 (0.0164)	0.0045	0.0652	68.2	0.6153 (0.0130)	0.6134 (0.0135)
3	0.6649 (0.0161)	0.6496 (0.0155)	0.0005	-0.0153	82.0	0.6111 (0.0139)	0.6042 (0.0137)	0.6467 (0.0157)	0.0006	-0.0181	77.0	0.6075 (0.0142)	0.6037 (0.0142)
4	0.6422 (0.0222)	0.6280 (0.0205)	0.0006	-0.0142	89.0	0.5988 (0.0262)	0.5879 (0.0247)	0.6303 (0.0216)	0.0006	-0.0119	93.0	0.5986 (0.0256)	0.5911 (0.0257)
Measurement error $\sigma_e^2 = 0.5$													
1	0.6947 (0.0176)	0.6722 (0.0198)	0.0009	-0.0225	80.2	0.6248 (0.0135)	0.6235 (0.0155)	0.6483 (0.0179)	0.0025	-0.0464	27.8	0.6067 (0.0138)	0.6060 (0.0137)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.6828 (0.0159)	0.6603 (0.0172)	0.0008	-0.0224	73.2	0.6175 (0.0142)	0.6133 (0.0136)	0.6 427 (0.0167)	0.0045	0.0652	32.0	0.6030 (0.0133)	0.6015 (0.0132)
3	0.6649 (0.0161)	0.6419 (0.0157)	0.0008	-0.0229	67.2	0.6055 (0.0142)	0.5985 (0.0138)	0.6335 (0.0156)	0.0012	-0.0314	47.4	0.5974 (0.0140)	0.5942 (0.0135)
4	0.6422 (0.0222)	0.6203 (0.0197)	0.0009	-0.0219	79.6	0.5937 (0.0256)	0.5814 (0.0232)	0.6206 (0.0208)	0.0009	-0.0216	84.0	0.5900 (0.0241)	0.5853 (0.0258)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.6947 (0.0176)	0.6626 (0.0216)	0.0015	-0.0321	68.6	0.6179 (0.0169)	0.6162 (0.0163)	0.6245 (0.0179)	0.0052	-0.0702	3.2	0.5892 (0.0134)	0.5887 (0.0136)
2	0.6828 (0.0159)	0.6520 (0.0187)	0.0013	-0.0308	62.4	0.6112 (0.0152)	0.6073 (0.0143)	0.6210 (0.0170)	0.0045	0.0652	4.6	0.5868 (0.0129)	0.5861 (0.0134)
3	0.6649 (0.0161)	0.6337 (0.0164)	0.0012	-0.0312	51.8	0.5997 (0.0148)	0.5922 (0.0140)	0.6151 (0.0157)	0.0027	-0.0498	10.8	0.5834 (0.0134)	0.5813 (0.0136)
4	0.6422 (0.0222)	0.6119 (0.0190)	0.0013	-0.0303	62.8	0.5874 (0.0239)	0.5753 (0.0223)	0.6059 (0.0197)	0.0017	-0.0363	53.2	0.5798 (0.0233)	0.5738 (0.0230)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.6947 (0.0176)	0.6560 (0.0230)	0.0020	-0.0387	60.2	0.6134 (0.0177)	0.6110 (0.0172)	0.6094 (0.0179)	0.0076	-0.0853	0.4	0.5780 (0.0133)	0.5780 (0.0134)
2	0.6828 (0.0159)	0.6469 (0.0200)	0.0017	-0.0359	57.6	0.6076 (0.0161)	0.6033 (0.0148)	0.6069 (0.0171)	0.0045	0.0652	0.8	0.5764 (0.0129)	0.5760 (0.0132)
3	0.6649 (0.0161)	0.6292 (0.0172)	0.0016	-0.0357	46.8	0.5958 (0.0149)	0.5894 (0.0147)	0.6026 (0.0159)	0.0041	-0.0622	2.6	0.5744 (0.0133)	0.5722 (0.0132)
4	0.6422 (0.0222)	0.6074 (0.0189)	0.0016	-0.0347	53.8	0.5826 (0.0240)	0.5734 (0.0226)	0.5954 (0.0190)	0.0025	-0.0468	30.4	0.5717 (0.0226)	0.5663 (0.0215)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.6947 (0.0176)	0.6514 (0.0240)	0.0025	-0.0442	53.8	0.6103 (0.0186)	0.6072 (0.0177)	0.6009 (0.0177)	0.0093	-0.0947	0.0	0.5722 (0.0132)	0.5715 (0.0129)
2	0.6828 (0.0159)	0.6432 (0.0206)	0.0021	-0.0404	51.8	0.6054 (0.0169)	0.6003 (0.0150)	0.5987 (0.0168)	0.0053	0.0706	0.2	0.5706 (0.0129)	0.5703 (0.0126)
3	0.6649 (0.0161)	0.6277 (0.0179)	0.0019	-0.0392	45.0	0.5947 (0.0155)	0.5888 (0.0143)	0.5955 (0.0163)	0.0054	-0.0714	1.0	0.5683 (0.0137)	0.5681 (0.0131)
4	0.6422 (0.0222)	0.6052 (0.0203)	0.0019	-0.0386	51.8	0.5806 (0.0247)	0.5720 (0.0244)	0.5892 (0.0188)	0.0033	-0.0547	20.8	0.5647 (0.0217)	0.5641 (0.0220)
Measurement error $\sigma_e^2 =$ 2.5													

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
1	0.6947 (0.0176)	0.6450 (0.0246)	0.0031	-0.0496	47.6	0.6058 (0.0190)	0.6024 (0.0180)	0.5908 (0.0180)	0.0111	-0.1039	0.0	0.5646 (0.0133)	0.5646 (0.0133)
2	0.6828 (0.0159)	0.6390 (0.0216)	0.0024	-0.0438	48.2	0.6019 (0.0173)	0.5975 (0.0158)	0.5893 (0.0174)	0.0090	-0.0935	0.2	0.5634 (0.0133)	0.5634 (0.0133)
3	0.6649 (0.0161)	0.6235 (0.0186)	0.0021	-0.0413	40.6	0.5914 (0.0159)	0.5856 (0.0149)	0.5866 (0.0162)	0.0064	-0.0783	0.2	0.5613 (0.0128)	0.5613 (0.0128)
4	0.6422 (0.0222)	0.6026 (0.0194)	0.0019	-0.0394	46.6	0.5791 (0.0240)	0.5699 (0.0223)	0.5813 (0.0182)	0.0040	-0.0607	9.6	0.5570 (0.0217)	0.5570 (0.0217)

Table S16: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 1$ and 50% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.7429 (0.0169)	0.7239 (0.0185)	0.0007	-0.0191	82.4	0.6658 (0.0869)	0.6614 (0.0153)	0.7053 (0.0176)	0.0017	-0.0377	43.8	0.6506 (0.0141)	0.6476 (0.0145)
2	0.7216 (0.0155)	0.7023 (0.0159)	0.0006	-0.0193	76.4	0.6519 (0.0140)	0.6424 (0.0134)	0.6916 (0.0158)	0.0012	-0.0300	51.8	0.6409 (0.0131)	0.6367 (0.0135)
3	0.6982 (0.0163)	0.6779 (0.0155)	0.0007	-0.0202	75.6	0.6349 (0.0142)	0.6230 (0.0146)	0.6758 (0.0156)	0.0007	-0.0224	71.4	0.6304 (0.0145)	0.6240 (0.0150)
4	0.6743 (0.0239)	0.6547 (0.0213)	0.0008	-0.0196	84.8	0.6201 (0.0235)	0.6052 (0.0232)	0.6591 (0.0228)	0.0008	-0.0152	90.8	0.6200 (0.0234)	0.6120 (0.0258)
Measurement error $\sigma_e^2 = 0.5$													
1	0.7429 (0.0169)	0.7148 (0.0200)	0.0012	-0.0281	69.2	0.6588 (0.0869)	0.6546 (0.0164)	0.6811 (0.0179)	0.0041	-0.0618	5.8	0.6316 (0.0140)	0.6299 (0.0143)
2	0.7216 (0.0155)	0.6935 (0.0170)	0.0011	-0.0281	60.2	0.6450 (0.0147)	0.6360 (0.0139)	0.6713 (0.0162)	0.0028	-0.0504	12.4	0.6251 (0.0132)	0.6218 (0.0134)
3	0.6982 (0.0163)	0.6688 (0.0158)	0.0011	-0.0294	52.8	0.6276 (0.0145)	0.6164 (0.0145)	0.6597 (0.0153)	0.0017	-0.0385	29.0	0.6173 (0.0145)	0.6130 (0.0141)
4	0.6743 (0.0239)	0.6450 (0.0204)	0.0013	-0.0293	68.0	0.6130 (0.0232)	0.5980 (0.0231)	0.6468 (0.0217)	0.0012	-0.0275	74.2	0.6107 (0.0223)	0.6031 (0.0252)
Measurement error $\sigma_e^2 = 1.0$													
1	0.7429 (0.0169)	0.7034 (0.0224)	0.0021	-0.0395	57.6	0.6503 (0.0869)	0.6457 (0.0174)	0.6508 (0.0181)	0.0088	-0.0921	0.2	0.6087 (0.0139)	0.6077 (0.0139)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.7216 (0.0155)	0.6840 (0.0189)	0.0018	-0.0376	47.2	0.6376 (0.0160)	0.6290 (0.0149)	0.6447 (0.0165)	0.0062	-0.0769	0.6	0.6047 (0.0131)	0.6029 (0.0132)
3	0.6982 (0.0163)	0.6595 (0.0166)	0.0018	-0.0387	25.0	0.6205 (0.0154)	0.6097 (0.0149)	0.6374 (0.0154)	0.0039	-0.0608	2.2	0.6000 (0.0135)	0.5974 (0.0139)
4	0.6743 (0.0239)	0.6350 (0.0197)	0.0019	-0.0393	48.6	0.6054 (0.0235)	0.5909 (0.0216)	0.6285 (0.0200)	0.0025	-0.0458	38.2	0.5958 (0.0218)	0.5910 (0.0233)
Measurement error $\sigma_e^2 = 1.5$													
1	0.7429 (0.0169)	0.6956 (0.0241)	0.0028	-0.0473	49.4	0.6477 (0.0871)	0.6394 (0.0183)	0.6320 (0.0180)	0.0126	-0.1109	0.0	0.5946 (0.0136)	0.5942 (0.0137)
2	0.7216 (0.0155)	0.6783 (0.0203)	0.0023	-0.0433	41.2	0.6334 (0.0171)	0.6247 (0.0157)	0.6277 (0.0167)	0.0091	-0.0939	0.0	0.5919 (0.0131)	0.5908 (0.0130)
3	0.6982 (0.0163)	0.6546 (0.0175)	0.0022	-0.0436	30.4	0.6167 (0.0159)	0.6063 (0.0151)	0.6225 (0.0155)	0.0060	-0.0757	0.0	0.5889 (0.0136)	0.5866 (0.0133)
4	0.6743 (0.0239)	0.6299 (0.0196)	0.0024	-0.0445	38.2	0.6018 (0.0243)	0.5871 (0.0202)	0.6156 (0.0191)	0.0038	-0.0588	13.4	0.5840 (0.0144)	0.5817 (0.0215)
Measurement error $\sigma_e^2 = 2.0$													
1	0.7429 (0.0169)	0.6902 (0.0259)	0.0035	-0.0534	46.2	0.6410 (0.0212)	0.6351 (0.0194)	0.6210 (0.0181)	0.0154	-0.1226	0.0	0.5870 (0.0136)	0.5859 (0.0134)
2	0.7216 (0.0155)	0.6767 (0.0218)	0.0028	-0.0481	41.6	0.6309 (0.0186)	0.6218 (0.0161)	0.6177 (0.0170)	0.0113	-0.1051	0.0	0.5845 (0.0132)	0.5838 (0.0130)
3	0.6982 (0.0163)	0.6532 (0.0187)	0.0025	-0.0468	32.0	0.6155 (0.0171)	0.6057 (0.0152)	0.6135 (0.0165)	0.0078	-0.0866	0.0	0.5815 (0.0142)	0.5809 (0.0139)
4	0.6743 (0.0239)	0.6270 (0.0209)	0.0027	-0.0477	35.2	0.5995 (0.0238)	0.5844 (0.0220)	0.6069 (0.0188)	0.0050	-0.0678	6.0	0.5789 (0.0211)	0.5756 (0.0212)
Measurement error $\sigma_e^2 = 2.5$													
1	0.7429 (0.0169)	0.6836 (0.0275)	0.0042	-0.0589	41.6	0.6364 (0.0222)	0.6297 (0.0205)	0.6093 (0.0182)	0.0181	-0.1333	0.0	0.5780 (0.0134)	0.5778 (0.0135)
2	0.7216 (0.0155)	0.6703 (0.0231)	0.0032	-0.0512	37.8	0.6277 (0.0193)	0.6184 (0.0173)	0.6068 (0.0172)	0.0135	-0.1148	0.0	0.5763 (0.0132)	0.5759 (0.0130)
3	0.6982 (0.0163)	0.6489 (0.0195)	0.0028	-0.0493	28.4	0.6127 (0.0174)	0.6018 (0.0159)	0.6035 (0.0162)	0.0092	-0.0948	0.0	0.5744 (0.0135)	0.5734 (0.0133)
4	0.6743 (0.0239)	0.6248 (0.0203)	0.0029	-0.0502	31.2	0.5983 (0.0243)	0.5832 (0.0202)	0.5986 (0.0183)	0.0062	-0.0764	1.0	0.5723 (0.0191)	0.5703 (0.0206)

Table S17: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 0$ and 70% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.5180 (0.0139)	0.5175 (0.0135)	0.0002	-0.0005	96.4	0.5124 (0.0097)	0.5124 (0.0096)	0.5178 (0.0138)	0.0002	-0.0002	95.6	0.5126 (0.0099)	0.5126 (0.0099)
2	0.5178 (0.0136)	0.5174 (0.0132)	0.0002	-0.0004	95.4	0.5122 (0.0099)	0.5124 (0.0096)	0.5176 (0.0135)	0.0002	-0.0002	95.6	0.5123 (0.0101)	0.5123 (0.0098)
3	0.5174 (0.0133)	0.5171 (0.0131)	0.0002	-0.0004	95.0	0.5107 (0.0137)	0.5136 (0.0117)	0.5172 (0.0133)	0.0002	-0.0002	95.0	0.5110 (0.0132)	0.5110 (0.0119)
4	0.5126 (0.0119)	0.5123 (0.0110)	0.0001	-0.0003	94.4	0.4554 (0.0732)	0.5641 (0.0708)	0.5124 (0.0111)	0.0001	-0.0002	95.6	0.4556 (0.0726)	0.5641 (0.0708)
Measurement error $\sigma_e^2 = 0.5$													
1	0.5180 (0.0139)	0.5174 (0.0136)	0.0002	-0.0005	95.6	0.5122 (0.0096)	0.5125 (0.0099)	0.5179 (0.0138)	0.0002	0.0000	94.6	0.5126 (0.0099)	0.5128 (0.0099)
2	0.5178 (0.0136)	0.5173 (0.0134)	0.0002	-0.0005	95.6	0.5122 (0.0099)	0.5123 (0.0099)	0.5178 (0.0135)	0.0002	0.0000	94.4	0.5124 (0.0102)	0.5128 (0.0098)
3	0.5174 (0.0133)	0.5170 (0.0133)	0.0002	-0.0004	95.6	0.5108 (0.0134)	0.5133 (0.0115)	0.5174 (0.0133)	0.0002	-0.0001	95.0	0.5114 (0.0133)	0.5133 (0.0117)
4	0.5126 (0.0119)	0.5123 (0.0111)	0.0001	-0.0003	94.4	0.4555 (0.0728)	0.5641 (0.0708)	0.5125 (0.0111)	0.0001	-0.0001	95.8	0.4558 (0.0720)	0.5641 (0.0708)
Measurement error $\sigma_e^2 = 1.0$													
1	0.5190 (0.0148)	0.5188 (0.0148)	0.0002	-0.0003	96.0	0.5133 (0.0106)	0.5133 (0.0107)	0.5187 (0.0145)	0.0002	-0.0004	95.0	0.5133 (0.0104)	0.5132 (0.0103)
2	0.5188 (0.0145)	0.5187 (0.0145)	0.0002	-0.0001	96.0	0.5131 (0.0107)	0.5135 (0.0106)	0.5185 (0.0141)	0.0002	-0.0003	95.4	0.5130 (0.0104)	0.5132 (0.0104)
3	0.5185 (0.0141)	0.5183 (0.0141)	0.0002	-0.0002	95.8	0.5124 (0.0145)	0.5136 (0.0118)	0.5180 (0.0138)	0.0002	-0.0005	95.2	0.5124 (0.0136)	0.5132 (0.0116)
4	0.5130 (0.0119)	0.5130 (0.0118)	0.0001	0.0000	94.4	0.4558 (0.0733)	0.5648 (0.0707)	0.5131 (0.0121)	0.0001	0.0001	96.0	0.4559 (0.0729)	0.5648 (0.0707)
Measurement error $\sigma_e^2 = 1.5$													
1	0.5201 (0.0160)	0.5192 (0.0148)	0.0002	-0.0009	96.0	0.5134 (0.0105)	0.5138 (0.0106)	0.5184 (0.0143)	0.0002	-0.0016	95.6	0.5132 (0.0102)	0.5129 (0.0103)
2	0.5197 (0.0157)	0.5193 (0.0146)	0.0002	-0.0004	95.4	0.5136 (0.0109)	0.5138 (0.0107)	0.5182 (0.0140)	0.0002	-0.0015	96.0	0.5129 (0.0102)	0.5129 (0.0104)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
3	0.5193 (0.0151)	0.5189 (0.0141)	0.0002	-0.0005	95.8	0.5124 (0.0144)	0.5144 (0.0123)	0.5178 (0.0136)	0.0002	-0.0016	95.4	0.5121 (0.0140)	0.5132 (0.0113)
4	0.5139 (0.0133)	0.5133 (0.0119)	0.0001	-0.0006	95.6	0.4562 (0.0735)	0.5647 (0.0706)	0.5128 (0.0119)	0.0001	-0.0012	96.0	0.4554 (0.0731)	0.5647 (0.0706)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5197 (0.0160)	0.5189 (0.0146)	0.0002	-0.0008	96.4	0.5133 (0.0105)	0.5134 (0.0104)	0.5182 (0.0142)	0.0002	-0.0015	96.4	0.5130 (0.0102)	0.5128 (0.0101)
2	0.5194 (0.0156)	0.5192 (0.0146)	0.0002	-0.0001	95.2	0.5135 (0.0107)	0.5138 (0.0108)	0.5181 (0.0139)	0.0002	-0.0013	95.2	0.5126 (0.0102)	0.5130 (0.0104)
3	0.5189 (0.0149)	0.5188 (0.0141)	0.0002	-0.0001	95.4	0.5125 (0.0140)	0.5143 (0.0122)	0.5176 (0.0134)	0.0002	-0.0013	95.4	0.5117 (0.0137)	0.5133 (0.0114)
4	0.5135 (0.0128)	0.5132 (0.0121)	0.0001	-0.0003	94.6	0.4577 (0.0735)	0.5629 (0.0702)	0.5127 (0.0119)	0.0001	-0.0008	94.6	0.4572 (0.0730)	0.5629 (0.0702)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.5194 (0.0153)	0.5190 (0.0151)	0.0002	-0.0004	95.6	0.5135 (0.0108)	0.5134 (0.0108)	0.5188 (0.0147)	0.0002	-0.0006	96.2	0.5133 (0.0105)	0.5133 (0.0105)
2	0.5191 (0.0149)	0.5195 (0.0153)	0.0002	0.0005	94.4	0.5138 (0.0114)	0.5140 (0.0111)	0.5186 (0.0144)	0.0002	-0.0005	95.8	0.5130 (0.0104)	0.5134 (0.0108)
3	0.5187 (0.0145)	0.5192 (0.0149)	0.0002	0.0004	94.8	0.5126 (0.0146)	0.5147 (0.0127)	0.5181 (0.0139)	0.0002	-0.0006	96.0	0.5120 (0.0138)	0.5138 (0.0120)
4	0.5132 (0.0125)	0.5135 (0.0126)	0.0002	0.0003	94.4	0.4557 (0.0738)	0.5656 (0.0710)	0.5134 (0.0129)	0.0002	0.0002	96.4	0.4555 (0.0736)	0.5656 (0.0710)

Table S18: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0.25 and 70% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.5695 (0.0224)	0.5640 (0.0222)	0.0005	-0.0055	94.2	0.5456 (0.0160)	0.5453 (0.0160)	0.5621 (0.0225)	0.0006	-0.0074	94.0	0.5442 (0.0162)	0.5440 (0.0161)
2	0.5686 (0.0219)	0.5633 (0.0216)	0.0005	-0.0054	94.0	0.5451 (0.0159)	0.5449 (0.0159)	0.5615 (0.0220)	0.0005	-0.0071	93.8	0.5436 (0.0163)	0.5439 (0.0161)
3	0.5663 (0.0219)	0.5610 (0.0211)	0.0005	-0.0054	94.6	0.5445 (0.0181)	0.5425 (0.0183)	0.5594 (0.0215)	0.0005	-0.0069	93.2	0.5427 (0.0185)	0.5420 (0.0180)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
4	0.5476 (0.0256)	0.5444 (0.0238)	0.0006	-0.0031	97.2	0.5079 (0.0803)	0.5618 (0.0683)	0.5436 (0.0245)	0.0006	-0.0039	97.4	0.5074 (0.0799)	0.5612 (0.0686)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.5695 (0.0224)	0.5612 (0.0224)	0.0006	-0.0083	93.4	0.5436 (0.0163)	0.5433 (0.0161)	0.5567 (0.0226)	0.0007	-0.0127	93.4	0.5404 (0.0163)	0.5402 (0.0162)
2	0.5686 (0.0219)	0.5604 (0.0218)	0.0005	-0.0082	91.0	0.5428 (0.0160)	0.5431 (0.0162)	0.5562 (0.0222)	0.0006	-0.0124	93.6	0.5398 (0.0163)	0.5401 (0.0162)
3	0.5663 (0.0219)	0.5580 (0.0211)	0.0005	-0.0083	91.6	0.5418 (0.0182)	0.5410 (0.0181)	0.5544 (0.0215)	0.0006	-0.0120	93.2	0.5390 (0.0181)	0.5386 (0.0183)
4	0.5476 (0.0256)	0.5422 (0.0229)	0.0006	-0.0054	96.8	0.5042 (0.0797)	0.5618 (0.0683)	0.5403 (0.0236)	0.0006	-0.0073	96.4	0.5025 (0.0791)	0.5606 (0.0682)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.5695 (0.0224)	0.5572 (0.0229)	0.0007	-0.0122	92.0	0.5408 (0.0166)	0.5405 (0.0165)	0.5493 (0.0226)	0.0009	-0.0202	84.8	0.5350 (0.0163)	0.5350 (0.0162)
2	0.5686 (0.0219)	0.5570 (0.0224)	0.0006	-0.0116	92.4	0.5406 (0.0167)	0.5404 (0.0163)	0.5489 (0.0223)	0.0009	-0.0197	84.6	0.5349 (0.0163)	0.5346 (0.0162)
3	0.5663 (0.0219)	0.5545 (0.0214)	0.0006	-0.0118	90.8	0.5396 (0.0186)	0.5384 (0.0176)	0.5474 (0.0214)	0.0008	-0.0190	84.8	0.5336 (0.0188)	0.5340 (0.0169)
4	0.5476 (0.0256)	0.5394 (0.0219)	0.0005	-0.0082	94.8	0.5007 (0.0796)	0.5606 (0.0681)	0.5354 (0.0223)	0.0006	-0.0122	94.4	0.4950 (0.0777)	0.5604 (0.0682)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.5695 (0.0224)	0.5544 (0.0233)	0.0008	-0.0151	90.8	0.5388 (0.0168)	0.5384 (0.0167)	0.5444 (0.0225)	0.0011	-0.0251	77.6	0.5316 (0.0161)	0.5314 (0.0161)
2	0.5686 (0.0219)	0.5547 (0.0230)	0.0007	-0.0139	91.0	0.5389 (0.0170)	0.5390 (0.0168)	0.5441 (0.0222)	0.0011	-0.0245	76.8	0.5313 (0.0162)	0.5313 (0.0161)
3	0.5663 (0.0219)	0.5525 (0.0219)	0.0007	-0.0139	90.0	0.5371 (0.0186)	0.5379 (0.0182)	0.5427 (0.0213)	0.0010	-0.0237	77.4	0.5304 (0.0184)	0.5306 (0.0169)
4	0.5476 (0.0256)	0.5378 (0.0217)	0.0006	-0.0098	94.0	0.4987 (0.0796)	0.5601 (0.0681)	0.5320 (0.0215)	0.0007	-0.0155	91.2	0.4904 (0.0774)	0.5595 (0.0679)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.5700 (0.0246)	0.5518 (0.0246)	0.0009	-0.0182	87.0	0.0014	-0.0296	0.0014	0.0014	-0.0296	70.8	0.5286 (0.0162)	0.5286 (0.0161)
2	0.5688 (0.0237)	0.5528 (0.0246)	0.0009	-0.0160	87.6	0.0013	-0.0287	0.0013	0.0013	-0.0287	71.2	0.5284 (0.0162)	0.5285 (0.0163)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
3	0.5656 (0.0223)	0.5504 (0.0235)	0.0008	-0.0152	88.6	0.0012	-0.0266	0.0012	0.0012	-0.0266	73.2	0.5276 (0.0182)	0.5280 (0.0177)
4	0.5479 (0.0254)	0.5362 (0.0226)	0.0006	-0.0117	94.0	0.0008	-0.0187	0.0008	0.0008	-0.0187	84.8	0.4869 (0.0759)	0.5585 (0.0666)
Measurement error $\sigma_e^2 = 2.5$													
1	0.5694 (0.0224)	0.5499 (0.0237)	0.0009	-0.0195	86.8	0.5366 (0.0172)	0.5353 (0.0168)	0.5381 (0.0218)	0.0015	-0.0313	65.8	0.5270 (0.0156)	0.5270 (0.0156)
2	0.5685 (0.0219)	0.5512 (0.0239)	0.0009	-0.0173	88.8	0.5364 (0.0180)	0.5365 (0.0170)	0.5379 (0.0215)	0.0014	-0.0307	66.4	0.5270 (0.0158)	0.5268 (0.0155)
3	0.5663 (0.0219)	0.5494 (0.0228)	0.0008	-0.0169	88.2	0.5349 (0.0193)	0.5358 (0.0191)	0.5367 (0.0206)	0.0013	-0.0296	65.4	0.5259 (0.0180)	0.5266 (0.0166)
4	0.5475 (0.0257)	0.5357 (0.0214)	0.0006	-0.0118	92.8	0.4955 (0.0796)	0.5599 (0.0681)	0.5276 (0.0201)	0.0008	-0.0200	81.0	0.4836 (0.0758)	0.5593 (0.0680)

Table S19: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 0.5$ and 70% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.6362 (0.0239)	0.6247 (0.0247)	0.0007	-0.0116	92.2	0.5892 (0.0181)	0.5891 (0.0183)	0.6196 (0.0238)	0.0008	-0.0166	89.6	0.5856 (0.0177)	0.5853 (0.0179)
2	0.6315 (0.0224)	0.6202 (0.0225)	0.0006	-0.0113	91.6	0.5869 (0.0174)	0.5851 (0.0174)	0.6164 (0.0227)	0.0007	-0.0150	89.2	0.5833 (0.0172)	0.5832 (0.0178)
3	0.6199 (0.0223)	0.6091 (0.0215)	0.0006	-0.0107	93.8	0.5805 (0.0203)	0.5764 (0.0192)	0.6076 (0.0223)	0.0006	-0.0122	91.2	0.5796 (0.0210)	0.5752 (0.0198)
4	0.5912 (0.0342)	0.5829 (0.0325)	0.0011	-0.0083	94.8	0.5600 (0.0726)	0.5683 (0.0604)	0.5832 (0.0339)	0.0012	-0.0080	94.4	0.5596 (0.0749)	0.5690 (0.0609)
Measurement error $\sigma_e^2 = 0.5$													
1	0.6362 (0.0239)	0.6190 (0.0251)	0.0009	-0.0172	89.2	0.5851 (0.0186)	0.5850 (0.0188)	0.6079 (0.0239)	0.0014	-0.0283	78.0	0.5770 (0.0176)	0.5769 (0.0177)
2	0.6315 (0.0224)	0.6147 (0.0232)	0.0008	-0.0168	88.8	0.5825 (0.0178)	0.5815 (0.0178)	0.6055 (0.0231)	0.0012	-0.0259	79.4	0.5758 (0.0172)	0.5749 (0.0178)
3	0.6199 (0.0223)	0.6036 (0.0215)	0.0007	-0.0163	89.0	0.5764 (0.0206)	0.5724 (0.0187)	0.5985 (0.0223)	0.0010	-0.0214	84.8	0.5720 (0.0209)	0.5695 (0.0192)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
4	0.5912 (0.0342)	0.5784 (0.0317)	0.0012	-0.0128	93.2	0.5534 (0.0716)	0.5676 (0.0603)	0.5772 (0.0326)	0.0013	-0.0140	92.6	0.5542 (0.0751)	0.5649 (0.0595)
Measurement error $\sigma_e^2 = 1.0$													
1	0.6362 (0.0239)	0.6113 (0.0262)	0.0013	-0.0250	83.4	0.5798 (0.0194)	0.5791 (0.0193)	0.5922 (0.0241)	0.0025	-0.0440	57.2	0.5656 (0.0177)	0.5657 (0.0176)
2	0.6315 (0.0224)	0.6082 (0.0245)	0.0011	-0.0233	84.2	0.5777 (0.0185)	0.5768 (0.0185)	0.5906 (0.0235)	0.0022	-0.0409	61.0	0.5646 (0.0169)	0.5645 (0.0183)
3	0.6199 (0.0223)	0.5974 (0.0222)	0.0010	-0.0224	84.2	0.5722 (0.0210)	0.5676 (0.0188)	0.5855 (0.0225)	0.0017	-0.0343	66.4	0.5628 (0.0196)	0.5598 (0.0195)
4	0.5912 (0.0342)	0.5736 (0.0306)	0.0012	-0.0176	92.4	0.5500 (0.0715)	0.5628 (0.0578)	0.5682 (0.0305)	0.0015	-0.0229	87.0	0.5438 (0.0732)	0.5611 (0.0578)
Measurement error $\sigma_e^2 = 1.5$													
1	0.6361 (0.0239)	0.6094 (0.0267)	0.0014	-0.0267	83.0	0.5784 (0.0197)	0.5778 (0.0197)	0.5889 (0.0249)	0.0029	-0.0473	52.6	0.5633 (0.0181)	0.5632 (0.0181)
2	0.6315 (0.0224)	0.6069 (0.0250)	0.0012	-0.0246	84.2	0.5768 (0.0189)	0.5758 (0.0190)	0.5874 (0.0242)	0.0025	-0.0441	57.2	0.5624 (0.0178)	0.5622 (0.0183)
3	0.6199 (0.0223)	0.5964 (0.0228)	0.0011	-0.0235	83.6	0.5715 (0.0217)	0.5669 (0.0192)	0.5827 (0.0231)	0.0019	-0.0372	64.8	0.5604 (0.0203)	0.5580 (0.0202)
4	0.5913 (0.0342)	0.5726 (0.0305)	0.0013	-0.0186	91.8	0.5488 (0.0713)	0.5625 (0.0579)	0.5660 (0.0301)	0.0015	-0.0252	86.2	0.5415 (0.0730)	0.5599 (0.0573)
Measurement error $\sigma_e^2 = 2.0$													
1	0.6348 (0.0218)	0.6005 (0.0263)	0.0019	-0.0343	74.8	0.5722 (0.0195)	0.5712 (0.0190)	0.5748 (0.0240)	0.0042	-0.0599	28.0	0.5533 (0.0175)	0.5531 (0.0173)
2	0.6304 (0.0211)	0.5999 (0.0253)	0.0016	-0.0305	77.0	0.5721 (0.0197)	0.5706 (0.0184)	0.5739 (0.0237)	0.0038	-0.0565	33.6	0.5529 (0.0177)	0.5523 (0.0174)
3	0.6209 (0.0213)	0.5917 (0.0232)	0.0014	-0.0292	75.0	0.5670 (0.0211)	0.5648 (0.0196)	0.5703 (0.0226)	0.0030	-0.0503	39.2	0.5508 (0.0199)	0.5504 (0.0190)
4	0.5877 (0.0359)	0.5665 (0.0286)	0.0013	-0.0212	86.6	0.5452 (0.0690)	0.5570 (0.0584)	0.5567 (0.0272)	0.0017	-0.0310	76.4	0.5319 (0.0693)	0.5548 (0.0574)
Measurement error $\sigma_e^2 = 2.5$													
1	0.6360 (0.0241)	0.5967 (0.0280)	0.0023	-0.0393	69.4	0.5694 (0.0206)	0.5685 (0.0202)	0.5684 (0.0244)	0.0052	-0.0676	20.4	0.5486 (0.0176)	0.5485 (0.0176)
2	0.6312 (0.0225)	0.5974 (0.0269)	0.0019	-0.0339	74.6	0.5701 (0.0202)	0.5688 (0.0201)	0.5676 (0.0239)	0.0046	-0.0636	22.8	0.5478 (0.0172)	0.5483 (0.0180)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
3	0.6196 (0.0223)	0.5889 (0.0244)	0.0015	-0.0308	75.0	0.5644 (0.0216)	0.5629 (0.0200)	0.5647 (0.0228)	0.0035	-0.0549	30.8	0.5461 (0.0194)	0.5463 (0.0189)
4	0.5911 (0.0344)	0.5679 (0.0299)	0.0014	-0.0232	86.0	0.5419 (0.0708)	0.5620 (0.0583)	0.5529 (0.0270)	0.0022	-0.0382	66.8	0.5227 (0.0695)	0.5583 (0.0569)

Table S20: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma =$ 0.75 and 70% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 =$ 0.25													
1	0.6949 (0.0213)	0.6789 (0.0229)	0.0008	-0.0161	90.0	0.6305 (0.0178)	0.6277 (0.0179)	0.6700 (0.0222)	0.0011	-0.0249	78.0	0.6231 (0.0169)	0.6221 (0.0174)
2	0.6825 (0.0208)	0.6665 (0.0211)	0.0007	-0.0160	87.0	0.6227 (0.0177)	0.6178 (0.0169)	0.6617 (0.0214)	0.0009	-0.0208	82.8	0.6180 (0.0175)	0.6153 (0.0172)
3	0.6640 (0.0228)	0.6478 (0.0219)	0.0007	-0.0162	89.4	0.6113 (0.0223)	0.6031 (0.0217)	0.6476 (0.0221)	0.0008	-0.0164	88.8	0.6089 (0.0216)	0.6047 (0.0219)
4	0.6266 (0.0408)	0.6143 (0.0385)	0.0016	-0.0122	93.4	0.5932 (0.0652)	0.5802 (0.0582)	0.6198 (0.0401)	0.0017	-0.0068	94.0	0.5965 (0.0663)	0.5854 (0.0594)
Measurement error $\sigma_e^2 =$ 0.5													
1	0.6949 (0.0213)	0.6710 (0.0242)	0.0012	-0.0239	82.6	0.6243 (0.0187)	0.6224 (0.0186)	0.6528 (0.0227)	0.0023	-0.0421	52.8	0.6103 (0.0169)	0.6093 (0.0176)
2	0.6825 (0.0208)	0.6588 (0.0218)	0.0010	-0.0237	82.0	0.6168 (0.0182)	0.6124 (0.0174)	0.6467 (0.0219)	0.0018	-0.0358	64.0	0.6065 (0.0175)	0.6043 (0.0174)
3	0.6640 (0.0228)	0.6401 (0.0219)	0.0010	-0.0238	80.4	0.6057 (0.0211)	0.5976 (0.0213)	0.6355 (0.0220)	0.0013	-0.0285	74.8	0.5991 (0.0208)	0.5966 (0.0217)
4	0.6266 (0.0408)	0.6076 (0.0362)	0.0017	-0.0190	90.4	0.5891 (0.0631)	0.5739 (0.0577)	0.6124 (0.0373)	0.0016	-0.0142	92.4	0.5887 (0.0633)	0.5822 (0.0598)
Measurement error $\sigma_e^2 =$ 1.0													
1	0.6949 (0.0213)	0.6605 (0.0261)	0.0019	-0.0344	72.2	0.6166 (0.0200)	0.6146 (0.0198)	0.6299 (0.0231)	0.0048	-0.0650	21.4	0.5934 (0.0173)	0.5926 (0.0173)
2	0.6825 (0.0208)	0.6501 (0.0231)	0.0016	-0.0324	71.2	0.6103 (0.0191)	0.6059 (0.0178)	0.6260 (0.0224)	0.0037	-0.0565	29.0	0.5909 (0.0177)	0.5897 (0.0174)
3	0.6640 (0.0228)	0.6319 (0.0224)	0.0015	-0.0320	68.0	0.5988 (0.0218)	0.5925 (0.0210)	0.6181 (0.0220)	0.0026	-0.0459	43.8	0.5863 (0.0207)	0.5839 (0.0209)

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
4	0.6266 (0.0408)	0.6000 (0.0338)	0.0018	-0.0265	88.0	0.5810 (0.0621)	0.5704 (0.0558)	0.6000 (0.0337)	0.0018	-0.0266	86.8	0.5768 (0.0603)	0.5747 (0.0577)
Measurement error $\sigma_e^2 =$ 1.5													
1	0.6946 (0.0217)	0.6520 (0.0284)	0.0026	-0.0426	67.0	0.6102 (0.0216)	0.6085 (0.0213)	0.6148 (0.0242)	0.0070	-0.0798	9.6	0.5822 (0.0178)	0.5819 (0.0180)
2	0.6827 (0.0206)	0.6440 (0.0255)	0.0021	-0.0387	67.4	0.6052 (0.0203)	0.6021 (0.0197)	0.6118 (0.0232)	0.0056	-0.0708	14.0	0.5803 (0.0176)	0.5797 (0.0180)
3	0.6631 (0.0229)	0.6259 (0.0239)	0.0020	-0.0372	64.8	0.5941 (0.0218)	0.5878 (0.0217)	0.6052 (0.0226)	0.0039	-0.0579	27.4	0.5758 (0.0200)	0.5754 (0.0206)
4	0.6260 (0.0392)	0.5962 (0.0326)	0.0019	-0.0297	84.6	0.5803 (0.0605)	0.5654 (0.0553)	0.5894 (0.0320)	0.0024	-0.0365	78.4	0.5718 (0.0610)	0.5638 (0.0560)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.6961 (0.0211)	0.6477 (0.0282)	0.0031	-0.0484	55.6	0.6072 (0.0215)	0.6050 (0.0213)	0.6050 (0.0234)	0.0088	-0.0911	2.6	0.5753 (0.0174)	0.5747 (0.0172)
2	0.6831 (0.0204)	0.6410 (0.0248)	0.0024	-0.0421	56.0	0.6033 (0.0205)	0.5994 (0.0184)	0.6028 (0.0228)	0.0070	-0.0803	5.4	0.5736 (0.0176)	0.5732 (0.0173)
3	0.6640 (0.0225)	0.6249 (0.0239)	0.0021	-0.0391	60.2	0.5933 (0.0230)	0.5874 (0.0216)	0.5975 (0.0223)	0.0049	-0.0665	15.6	0.5704 (0.0203)	0.5697 (0.0202)
4	0.6269 (0.0410)	0.5941 (0.0319)	0.0021	-0.0328	83.0	0.5758 (0.0639)	0.5665 (0.0551)	0.5834 (0.0301)	0.0028	-0.0435	68.4	0.5637 (0.0592)	0.5621 (0.0549)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.6952 (0.0233)	0.6399 (0.0307)	0.0040	-0.0553	56.8	0.6016 (0.0233)	0.5993 (0.0226)	0.5953 (0.0246)	0.0106	-0.0999	1.4	0.5679 (0.0179)	0.5678 (0.0180)
2	0.6825 (0.0214)	0.6361 (0.0280)	0.0029	-0.0464	62.4	0.5994 (0.0219)	0.5961 (0.0212)	0.5933 (0.0236)	0.0085	-0.0893	2.8	0.5666 (0.0174)	0.5664 (0.0182)
3	0.6622 (0.0236)	0.6205 (0.0260)	0.0024	-0.0417	60.8	0.5903 (0.0239)	0.5832 (0.0219)	0.5891 (0.0223)	0.0058	-0.0731	8.8	0.5647 (0.0202)	0.5630 (0.0198)
4	0.6252 (0.0383)	0.5929 (0.0338)	0.0022	-0.0323	83.6	0.5774 (0.0620)	0.5631 (0.0539)	0.5752 (0.0301)	0.0034	-0.0500	61.8	0.5570 (0.0600)	0.5567 (0.0511)

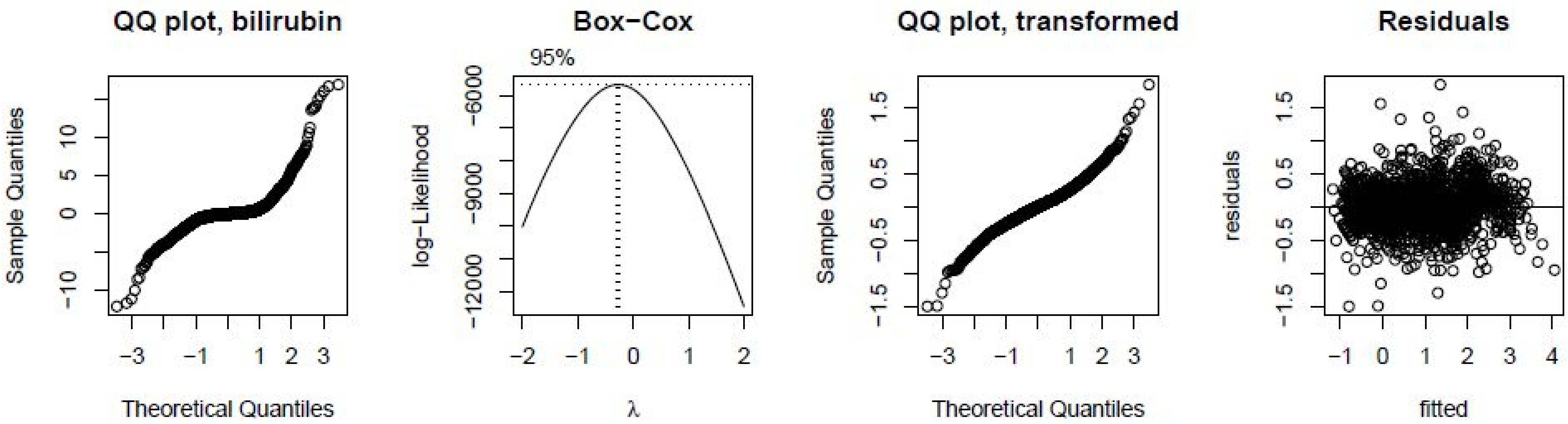
Table S21: Time-dependent AUC, sensitivity, specificity at t_h for the measurement error adjusted and observed biomarkers when $\gamma = 1$ and 70% censoring

t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
Measurement error $\sigma_e^2 = 0.25$													
1	0.7431 (0.0214)	0.7228 (0.0236)	0.0010	-0.0203	86.4	0.6650 (0.0194)	0.6608 (0.0192)	0.7100 (0.0227)	0.0016	-0.0330	69.8	0.6544 (0.0184)	0.6513 (0.0184)
2	0.7209 (0.0204)	0.7004 (0.0207)	0.0009	-0.0206	83.8	0.6507 (0.0182)	0.6413 (0.0176)	0.6950 (0.0206)	0.0011	-0.0260	76.4	0.6444 (0.0173)	0.6389 (0.0178)
3	0.6942 (0.0240)	0.6739 (0.0228)	0.0009	-0.0203	85.6	0.6337 (0.0226)	0.6198 (0.0232)	0.6757 (0.0234)	0.0009	-0.0185	88.2	0.6324 (0.0230)	0.6235 (0.0235)
4	0.6581 (0.0394)	0.6412 (0.0371)	0.0017	-0.0169	93.4	0.6180 (0.0573)	0.5951 (0.0509)	0.6486 (0.0404)	0.0017	-0.0095	94.6	0.6202 (0.0591)	0.6042 (0.0558)
Measurement error $\sigma_e^2 = 0.5$													
1	0.7431 (0.0214)	0.7133 (0.0254)	0.0015	-0.0298	79.0	0.6577 (0.0207)	0.6536 (0.0204)	0.6877 (0.0233)	0.0036	-0.0554	31.2	0.6366 (0.0182)	0.6349 (0.0185)
2	0.7209 (0.0204)	0.6914 (0.0218)	0.0013	-0.0295	73.6	0.6437 (0.0188)	0.6346 (0.0180)	0.6765 (0.0209)	0.0024	-0.0445	43.2	0.6292 (0.0176)	0.6259 (0.0171)
3	0.6942 (0.0240)	0.6650 (0.0227)	0.0014	-0.0292	75.0	0.6257 (0.0225)	0.6141 (0.0225)	0.6619 (0.0227)	0.0016	-0.0324	70.0	0.6204 (0.0222)	0.6145 (0.0219)
4	0.6581 (0.0394)	0.6329 (0.0354)	0.0019	-0.0252	90.0	0.6095 (0.0560)	0.5903 (0.0493)	0.6391 (0.0389)	0.0019	-0.0190	93.0	0.6104 (0.0582)	0.5992 (0.0529)
Measurement error $\sigma_e^2 = 1.0$													
1	0.7424 (0.0206)	0.7002 (0.0265)	0.0025	-0.0422	86.4	0.6478 (0.0214)	0.6435 (0.0207)	0.6590 (0.0227)	0.0075	-0.0834	69.8	0.6151 (0.0173)	0.6137 (0.0175)
2	0.7211 (0.0200)	0.6817 (0.0231)	0.0021	-0.0395	83.8	0.6363 (0.0199)	0.6274 (0.0188)	0.6524 (0.0218)	0.0052	-0.0687	76.4	0.6105 (0.0175)	0.6089 (0.0179)
3	0.6961 (0.0246)	0.6569 (0.0231)	0.0021	-0.0392	85.6	0.6200 (0.0237)	0.6085 (0.0214)	0.6424 (0.0225)	0.0034	-0.0537	88.2	0.6036 (0.0211)	0.6023 (0.0216)
4	0.6562 (0.0427)	0.6224 (0.0334)	0.0023	-0.0338	93.4	0.6007 (0.0549)	0.5829 (0.0519)	0.6244 (0.0353)	0.0023	-0.0318	94.6	0.6001 (0.0526)	0.5874 (0.0505)
Measurement error $\sigma_e^2 = 1.5$													
1	0.7430 (0.0210)	0.6914 (0.0293)	0.0035	-0.0516	58.8	0.6414 (0.0236)	0.6364 (0.0225)	0.6410 (0.0238)	0.0110	-0.1020	1.0	0.6012 (0.0177)	0.6009 (0.0182)

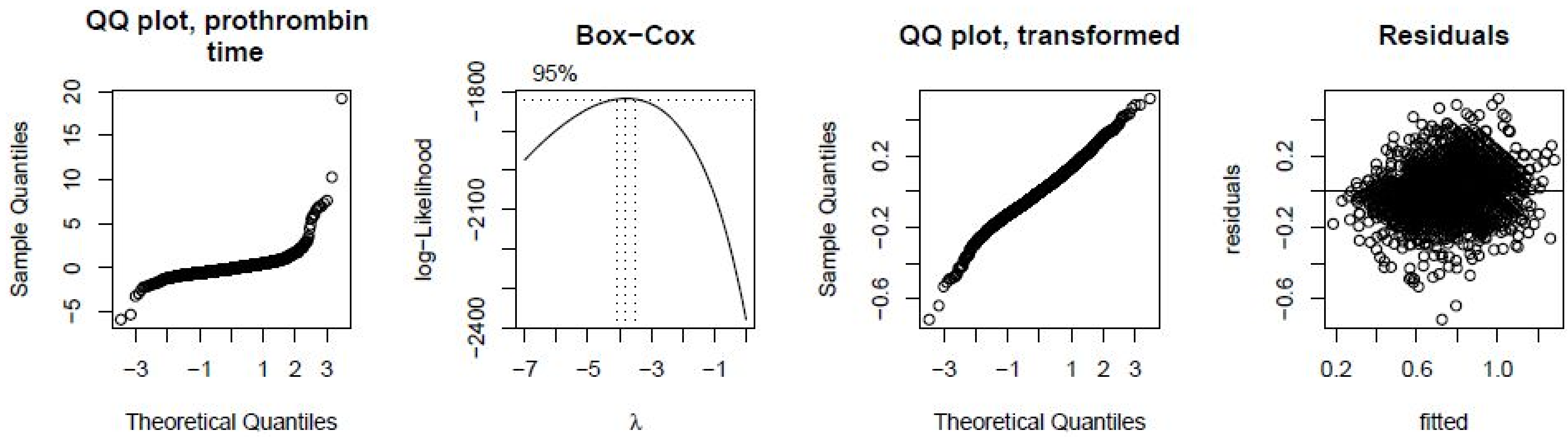
t_h	True AUC (SE)	Measurement error Adjusted						Observed					
		AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)	AUC (SE)	MSE	Bias	Cov	Sensitivity (SE)	Specificity (SE)
2	0.7212 (0.0203)	0.6750 (0.0257)	0.0028	-0.0461	57.6	0.6311 (0.0217)	0.6223 (0.0200)	0.6353 (0.0222)	0.0079	-0.0859	1.8	0.5975 (0.0178)	0.5963 (0.0172)
3	0.6964 (0.0246)	0.6533 (0.0242)	0.0024	-0.0431	56.4	0.6169 (0.0236)	0.6054 (0.0225)	0.6291 (0.0228)	0.0050	-0.0673	15.0	0.5947 (0.0215)	0.5912 (0.0215)
4	0.6563 (0.0407)	0.6190 (0.0329)	0.0025	-0.0373	81.6	0.5954 (0.0539)	0.5829 (0.0505)	0.6102 (0.0328)	0.0032	-0.0461	71.8	0.5860 (0.0525)	0.5794 (0.0506)
Measurement error $\sigma_e^2 =$ 2.0													
1	0.7425 (0.0216)	0.6829 (0.0320)	0.0046	-0.0596	51.6	0.6348 (0.0256)	0.6307 (0.0242)	0.6278 (0.0244)	0.0137	-0.1147	0.4	0.5917 (0.0182)	0.5913 (0.0182)
2	0.7206 (0.0207)	0.6690 (0.0273)	0.0034	-0.0516	50.0	0.6260 (0.0227)	0.6186 (0.0213)	0.6233 (0.0226)	0.0100	-0.0973	0.8	0.5886 (0.0173)	0.5878 (0.0173)
3	0.6943 (0.0248)	0.6468 (0.0263)	0.0029	-0.0475	53.8	0.6117 (0.0252)	0.6014 (0.0233)	0.6173 (0.0234)	0.0065	-0.0771	8.2	0.5855 (0.0220)	0.5833 (0.0214)
4	0.6573 (0.0421)	0.6154 (0.0325)	0.0028	-0.0419	73.0	0.5946 (0.0503)	0.5779 (0.0482)	0.6044 (0.0321)	0.0038	-0.0529	58.8	0.5808 (0.0479)	0.5763 (0.0483)
Measurement error $\sigma_e^2 =$ 2.5													
1	0.7418 (0.0209)	0.6769 (0.0335)	0.0053	-0.0649	48.2	0.6302 (0.0269)	0.6262 (0.0254)	0.6169 (0.0240)	0.0162	-0.1249	0.0	0.5838 (0.0179)	0.5832 (0.0177)
2	0.7196 (0.0194)	0.6647 (0.0276)	0.0038	-0.0549	49.2	0.6229 (0.0238)	0.6151 (0.0217)	0.6131 (0.0225)	0.0119	-0.1065	0.4	0.5815 (0.0171)	0.5804 (0.0175)
3	0.6959 (0.0237)	0.6457 (0.0276)	0.0033	-0.0502	51.8	0.6101 (0.0259)	0.6009 (0.0241)	0.6087 (0.0232)	0.0081	-0.0872	3.0	0.5796 (0.0202)	0.5771 (0.0212)
4	0.6580 (0.0388)	0.6123 (0.0352)	0.0033	-0.0458	73.8	0.5893 (0.0553)	0.5785 (0.0486)	0.5965 (0.0308)	0.0047	-0.0615	46.6	0.5716 (0.0481)	0.5733 (0.0476)

Application: Mayo Clinic primary biliary cirrhosis (PBC) study

Bilirubin: Were log-transformed. A linear trajectory is assumed in the longitudinal data sub-model, and the residual plot does not indicate any deviations from a linear form.



Prothrombin time: Transformed by (0.1×prothrombin time)-4 as suggested by Box-Cox transformation. A linear trajectory is assumed in the longitudinal data sub-model, and the residual plot does not indicate any deviations from a linear form.



Albumin: Did not require transformation as suggested by Box-Cox transformation. A linear trajectory is assumed in the longitudinal data sub-model, and the residual plot does not indicate any deviations from a linear form.